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MEDICAL RESEARCH COMMITTEE.

Special Report Series

REPORTS

OF THE

CHEMICAL WARFARE MEDICAL COMMITTEE.

No. 1. NOTES ON THE PATHOLOGY AND TREATMENT OF THE EFFECTS OF PULMONARY IRRITANT GASES.

Compiled by the Physiology (War) Committeee of the Royal Society, September, 1917, and adopted by the Chemical Warfare Medical Committee, January, 1918.

In January, 1918, the Director-General, Army Medical Service, with the concurrence of the Controller of Chemical Warfare, appointed the following Committee to prepare reports, based upon information received from all sources at the Chemical Warfare Department, for submission to him with a view to their distribution to those concerned, to make suggestions for further co-ordinated medical investigations that may seem desirable, and to advise him generally in respect of the scientific medical aspects of Chemical Warfare :—

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N.B.—*The Appendices referred to in the present report will appear in subsequent reports.*

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PHYSIOLOGY (WAR) COMMITTEE OF THE ROYAL SOCIETY.

September, 1917.

NOTES ON THE PATHOLOGY AND TREATMENT OF THE EFFECTS OF PULMONARY IRRITANT GASES.

Preliminary.

The action of those gases and vapours which may be described as *pulmonary irritants* is to cause changes which are generally not conspicuously evident till some hours have elapsed. There are cases, however, in which, experimentally, practically immediate death has been brought about. Field experiments have shown that a rat and rabbit placed about five yards from, and to leeward of, a bomb containing phosgene were found dead within eight minutes after its explosion. Control animals similarly situated to windward died after several hours. Other controls, in which shells filled with water instead of toxic substances were used, have shown that the concussion must not be regarded as a cause of death.

Similar results have been obtained in laboratory experiments at Cambridge and elsewhere. Mice exposed to a high concentration of phosgene in a small closed chamber may die during the third minute. (*Barcroft.*)

Autopsies of such animals show intense venous and capillary congestion, and subdural hæmorrhages have been observed upon the brain. The lungs showed practically no œdema. The blood vessels of the lungs were much congested and inundated with a brownish granular material suggesting considerable decomposition of the hæmoglobin. The blood in the systemic circulation was normal to spectroscopic examination. Clearly animals can be killed immediately by exposure to a sufficient concentration of phosgene. The evidence indicates that death is accompanied by, and probably due to, an immediate pulmonary vascular stasis resulting in acute asphyxia.

French observers have found that immediate death, with profound lung changes, may be brought about by chlorine of high concentration. (*Paris Conference, May* 28, 1917). Cats exposed to chlorine, 1 in 700 or even less, as 1 in 2,500, have been killed in less than fifteen minutes, the blood being almost black, the arterial pressure falling rapidly without asphyxial rise and there being practically no lung œdema. (*Bayliss.*) The question has been asked whether early death (i.e., within two hours) may occur, after gassing, without any changes in the lungs.

There appears to be no evidence for this. Pulmonary changes appears to be a necessary stage in all the pathological effects of the irritant gases to be mentioned below. With doses of such strength as to cause death in two hours, damage to the lung would seem to be a necessary factor in the train of pathological symptoms. The question whether gases like chlorine and phosgene have toxic effects independent of the direct damage they can effect in the lungs will be discussed later.

Extended experience of gas warfare compels us to recognise that there are two varieties of pulmonary irritant gases. In the first variety, of which phosgene may be regarded as a type, the lung alveoli are mainly affected, with consequent œdema of the lungs and great interference with absorption of oxygen. In the second variety, of which dichlorethylsulphide is a type, the air-passages are mainly affected, and there is little or no œdema of the lungs, but urgent danger to life may arise from mechanical blocking of the air-passages. There are, however, many gases which, like chlorine, act markedly on both the alveoli and air-passages. In all cases the local inflammation and necrosis affords opportunity for the development of infections which may lead to infective bronchitis and broncho-pneumonia, particularly in the second variety of pulmonary irritants.

Why it is that some substances appear to attack the air passages, others the alveoli, may to some extent be explained. When the substance is introduced in the "atomised" condition, if the spray be coarse, it may be entirely held up by the air passages. A very fine spray would have a better chance of reaching the alveoli, and would presumably then produce the condition of alveolar œdema, absent ordinarily with such a substance as methyl sulphate. If the substance is very soluble, as ammonia, the moisture of the surface of the air passages would largely entrap it. Beyond this it may be possible that a substance is comparatively innocuous to the more resistant epithelium of the air passages and only effective upon the delicate alveolar epithelium, as in the case of phosgene. Or finally, it may be that the vapour has some peculiar affinity for some tissues whilst it is relatively indifferent to others, so that the epithelium of the air passages is attacked but not the alveolar epithelium even if the vapour reaches it, as with dichlorethylsulphide. The ease with which the substance is decomposed and its concentration are factors which will again be of importance in determining its seat of action.

(A).—PATHOLOGICAL.

(i) Pulmonary Changes.

(Edema: time of onset in relation to concentration.—The rapidity and severity with which œdema is produced is commonly found to vary, as would be expected, in some direct relation to the concentration of gas used and the duration of exposure to it. French observations indicate that a characteristic curve may be plotted for each gas, relating the two factors of concentration and time of exposure, with reference to its effectiveness in causing death.

Changes in the tissues of the lung and their relation to œdema.—If judged by the signs of fluid collecting in the alveoli, or the amount of fluid escaping by the bronchi, the onset of œdema may be either immediate, in the sense that it begins rapidly after exposure to gas, or delayed, in the sense that a considerable latent period, even of several hours, may pass, after the time of exposure, before obvious signs of œdema appear.

The fact that water is constantly being evaporated from the alveolar walls implies the conception of a normal mechanism which continuously bathes the epithelium with lymph and further provides for drainage of lymph from the alveolar walls. There is always an outflow of liquid which is balanced by the activity of the drainage mechanism. One must regard lymphatics of origin as normally existent in the substance of the alveolar walls from which more definite lymphatic vessels arise and lead to various lymphatic systems. These are mainly in the pulmonary pleural membrane, in the interlobular connective tissue or the connective tissue around the blood-vessels and bronchi. In some animals, as in the rabbit, the drainage system from the alveoli is mainly by the periarterial lymphatics. In man and most animals the pleural and interlobular lymphatics are also prominent as the drainage path from the alveolar walls. Normally the effectiveness of this drainage mechanism is such that there is no accumulation of lymph in the air spaces or the substance of the walls. But if there be any factor leading to excessive production the normal drainage may be insufficient, hence an accumulation of lymph, i.e., œdema, occurs. If the cause of increased production does not persist, drainage may overtake and gradually overcome the accumulation. Excessive production and accumulation may also occur as the result of damage. The normal boundaries to the lymphatics of the walls may be injured and a leakage may occur into the air spaces or the effect of toxic substances may be such as to increase the permeability of the pulmonary capillaries, and in this way an increased exudation may arise. In either manner the balance between production and drainage may be upset. It seems likely that any cause that brings about a rise in the pulmonary blood-pressure, such as exercise, will lead to a more intense production. It follows from these considerations that the rate at which œdema develops may vary. Augmented drainage may compensate for a slightly increased production, and no œdema may occur. The stimulus to production may not persist though strong enough at first to lead to some œdema. The persistence of the augmented reabsorption may cause the gradual removal of the excess so that later no œdema is to be found. The destruction of the alveolar epithelium or other alveolar tissue may be only slowly brought about and thus a real latent period may occur, in which the primary change wrought in the epithelium does not in its first stages allow increased exudation, which is only permitted as the result of some secondary sequence of intracellular changes which may lead to a later damage or death of the cell structure. Finally, the presence of even slight excess of fluid on the alveolar surface impairs the gaseous exchange and leads to oxygen lack in the tissues generally; under

conditions of warmth and rest this may not develop to any serious degree, but with exercise, the increased respiratory movements (even though these may augment the process of reabsorption) and the rise of blood pressure in the pulmonary vessels, may possibly lead to such increased production of lymph as to develop œdema, and this, interfering with the gaseous exchange, would diminish the intake of oxygen when the blood is most in need of it. Further, independently of enhanced production, the respiratory movements would tend to drive œdema fluid into the bronchi and cause mechanical blocking of certain areas.

The above views are largely the result of a study of the different appearances presented by the lungs of animals exposed for different periods to varying concentrations of phosgene. With the same sublethal dose, animals killed at different periods after exposure give a staged representation of the conditions that practically uniformly develop. There may be in the earliest hours no alveolar œdema, but slightly distended lymphatics. Later, some alveolar œdema, but much more distended lymphatics. In from twelve to twenty-four hours intense alveolar œdema and markedly distended lymphatics. Sometimes the alveolar œdema is almost absent but the lymphatics are strikingly engorged. In cases where exercise has proved fatal in animals alveolar œdema without marked engorgment of lymphatics has been very evident. (*Edkins & Tweedy.*)

The amount of œdema fluid accumulated in the lungs in one fatal human case has been estimated at about a litre—that is about one-fifth of the blood. (*Elliott.*) In a fatal case of phosgene poisoning over two litres of liquid have been coughed up in an hour and a quarter. (*Haldane.*) In a rabbit which was not fatally gassed the fluid was 21 c.c.—perhaps about one-eighth of the volume of the blood. (*Dufton.*) A goat may have even a kilo. of fluid amounting to three to four-fifths of the blood volume. (*Porton observation.*)

In numerous cases of poisoning with chloropicrin, a considerable quantity of fluid in the pleural and pericardial cavities has been found in addition to the œdema. In some of these cases there was but little œdema.

The degree of pulmonary œdema has been estimated by various methods. The French observers take a given weight of lung, mince it, centrifugalize and so find the ratio of solids to fluid. In England the amount of œdema has been expressed in terms of the alteration of the weight-ratio of heart to lungs, the normal in most animals being 1 : 1·5, in goats about 1 : 2. The latter method seems preferable for it takes account of the total changes. The former method depends on sampling and the irregular distribution of œdema in the lungs makes sampling unreliable. (*Barcroft.*)

The intensity of the œdema production at times is suggested by such observations as the following :—After exposure to strong doses of gas the excised œdematous lung is at first distended by the alveolar fluid almost to the volume it occupied before the thorax was opened. It gradually shrinks by its elastic tissue squeezing out the fluid, and finally lies in a bath of the expressed liquid, like a clot in serum. It

has been noted also that in lung-heart preparations, especially if a main bronchus is obstructed, fluid will drain out from the pulmonary pleural membrane, and the lung is finally found to be floating in an accumulation of fluid more or less filling the pleural cavity. (*L. Hill.*)

In animal experiments some attention has been directed to the early local changes in the lungs in respect of cell invasions. Within an hour or two the number of polymorphs in the blood-vessels is greatly increased. Lymphocytes do not seem to show this increase to the same degree. The polymorpholeucocytosis, sometimes remarkably intense, is usually temporary, and during its persistence the polymorphs undergo considerable and characteristic changes. They pass abundantly into the œdema fluid and may influence its reabsorption. Somewhat later than the invasion of polymorphs and reaching a maximum at about the third day after gassing a conspicuous feature is the appearance of large mono-nuclear cells which have budded from the alveolar epithlieum. These have active phagocytic power and remains of polymorphs and erythrocytes can be frequently recognised. They almost invariably contain dark granules which are not carbon but of hæmosiderin origin. At a later period (five days) the prominent feature is an invasion of true eosinophils. At times the polymorphs do not diminish but remain in conspicuous clumps simulating the formation of local abscesses. (*Edkins & Tweedy.*)

Changes in Pulmonary Blood-vessels.—In cases of poisoning with phosgene which are too slight to show actual microscopic evidence of epithelial changes, general vascular congestion is observable.

Where the poison is stronger, there are well-marked large patches of alveolar œdema. The blood, however, coming from lungs in which these are present may be perfectly oxygenated. The assumption, therefore, is that the circulation through the œdematous patches has become insignificant in quantity. For otherwise, much venous blood would be mixed up with the oxygenated blood, and the whole blood reaching the heart from the lung would be only partially oxygenated.

The alveolar vascular congestion is continued for some days, but this is much less obvious when the alveoli are choked with the cellular material above described. In some cases there appears to be an absolute blocking of capillaries by closely massed erythrocytes. Thrombosis of capillaries has been frequently observed in man, sometimes in large areas around damaged infundibula. Occasionally a true thrombosis in the larger pulmonary vessels may be seen and at times peripheral thrombosis in vessels other than capillaries. (*Dunn.*)

Injected specimens of gassed lungs are as yet few. The injected vessels are singularly un-uniform. This may, however, be due to defective injection. Further observations on this point are being made and experiments on the resistance of the vascular area of gassed lungs to perfusion fluids are in progress.

Bronchial Spasm.—In cases of accidental "gassing" by phosgene or chloropicrin in factories, a frequent and distressing symptom is spasmodic asthma, which may occur even after brief inhalations of small quantities of vapour. Well-marked constriction of the bronchioles has been observed as the result of inhalation of phosgene in animals.

(*Golla.*) Exposure to chlorine has not been observed experimentally to produce this effect. (*Bayliss.*) It is not yet clear how far and for how long, bronchial spasm may occur in men gassed in warfare. Laryngeal spasm may sometimes have been confused with bronchial spasm in man.

Resultant Interference with Respiratory Exchanges.—General and severe damage to the lung epithelium and capillaries entails rapidly developing œdema. Such alveolar œdema necessarily interferes with the respiratory exchanges in the lungs. During the asphyxial condition thus established, tearing of the alveolar walls may be produced both in œdematous and unflooded areas of the lung by convulsive efforts at breathing. This tearing which is specially evident in lungs of animals gassed with chlorine (causing laryngeal spasm and perhaps bronchial constriction) still further reduces the available respiratory area.

In man the lungs, after fatal damage by irritant gas, usually show very extensive areas of emphysema due to tearing of the alveolar walls by the respiratory efforts, alternating with areas of partial or complete collapse in addition to areas extensively flooded by œdema fluid. When the œdema is not intense the subjects may exhibit definite hyperpnœa with little or no cyanosis, and signs of urgent oxygen want appear absent. If the œdema is comparatively intense or the distribution of the œdema lead to sound areas becoming blocked, then the absorption of oxygen is seriously interfered with. The subjects present symptoms of grave anoxæmia, but the output of CO_2 may or may not be hampered. If it is hampered, there is profound cyanosis, the result primarily of the oxygen want, accompanied by a full pulse and distension of the veins. The subject exhibits, in this case, a full blue or plum-coloured cyanosis. The immediate danger here is the anoxæmia, on account of the great susceptivility of the heart and central nervous system to deficiency of oxygen. On the other hand the anoxœmia may be unaccompanied by marked increase of CO_2 tension in the blood. The subject is ashy-grey in colour and shows no intense breathlessness. He may even seem to be fairly comfortable, this being due, in part probably, to the narcotic effect of oxygen want. In spite of the lack of distress, however, the condition is one of the utmost gravity.*

Haldane has described the functional condition as follows (" B.M.J.," Feb. 10, 1917) :—

" In acute inflammatory conditions of the lungs there is sometimes also want of oxygen, as shown by cyanosis ; and where the inflammatory condition is accompanied by the presence of " œdematous " exudation throughout the lungs the cyanosis is often very great. This condition is seen typically in the acute stages of poisoning by nitrous fumes or chlorine. What is its probable cause ? When a portion of the lungs, including even the greater part of both lungs, is entirely blocked by consolidation, as in croupous pneumonia there is commonly on cyanosis. This indicates that very little blood is passing through the consolidated parts. What passes through the healthy portion is

* Compare " *A Fatal Case of Phosgene Poisoning* " in Appendix of Reports.

amply sufficient for respiratory requirements during rest. It must be borne in mind that the normal lungs and circulatory organs are adapted for meeting about ten times the respiratory requirements during rest, since the respiratory exchange is often about ten times as great during work as during rest. Hence during rest in bed a very small proportion of normal lung will suffice for meeting respiratory and circulatory requirements, provided there is but little circulation through parts which are useless. But when cyanosis due to a lung affection exists, in spite of the fact that air is entering the whole or a great part of the lungs freely, we seem driven to the conclusion that the entry of oxygen into the blood through the alveolar walls is impeded by exudation and increase in thickness of the alveolar walls.

It is very important to realize that this may occur without any serious impediment to the passage of CO_2 outwards. CO_2 is about twenty-five times as soluble in water as oxygen, and hence it passes through the alveolar walls far more easily, with a given difference of partial pressure, than does oxygen. Moreover, a comparatively slight increase in the breathing will enormously increase the small difference in diffusion pressure on which the passage of CO_2 outwards depends ; but the same increase in breathing produces only a slight proportional increase in the diffusion pressure which drives oxygen inwards. Hence we may have cyanosis, and consequently very formidable effects from oxygen want, without marked hyperpnœa. The grey look of the patient's face will be a good index of this. There will probably be no increase of venous blood pressure with its accompanying full blue cyanosis."

When the damage is such as only to diminish the lung surface available for gaseous interchange, as in marked emphysema or blocking of the circulation in complete areas, the opportunity for CO_2 diffusion is lessened and the CO_2 pressure in the blood and tissues may rise. In such cases there may be no oxygen want as long as the subject is at rest. Haldane has pointed out that a very slight rise in CO_2 tension in the blood will produce hyperpnœa. Such cases will be normal in colour and only exhibit breathlessness.

For the practical purposes of treatment, to be discussed below, in which an increase of the oxygen supply and a diminution of the oxygen demand by bodily rest and warmth are the cardinal points, a closer analysis of physiological details is hardly called for. Experiments on animals indicate that the normal oxygenation of the blood may be effected, even in the presence of œdema. But it is difficult or impossible with moderate concentrations of gas to produce uniform effects in all parts of the lung, and there is no doubt that in spite of local œdema, the undamaged areas of the lung can carry on, for a time, an adequate exchange. But if some extra demand is made for oxygen, as by an increase in muscular work, or if previously open areas become flooded by œdema fluid, or, finally, if the air entry into open areas is obstructed by fluid dislocated from alveoli that are waterlogged, then an adequate intake of oxygen is no longer possible.

Respiratory Centre.—In fatal delayed cases of phosgene poisoning, the respiratory centre is much depressed in rabbits, and its failure appears to be the ultimate cause of death. Asphyxia in such animals

does not produce either the typical changes in respiration or in blood pressure. (*Barcroft.*)

In human cases the respiratory centre appears to retain its physiological activity until a phase is reached of definite oxygen want. In mild cases of gassing, the centre responds normally by hyperpnœa to the increased CO_2 tension, and may so preserve the balance as to leave the face its usual colour and give no symptom of distress. With greater lung damage, whether immediate or delayed, the centre may respond, again physiologically, and give dyspnœa, with visible cyanosis, accompanied, as asphyxia advances, by venous congestion. As mentioned below, oxygen want as it progresses lowers the irritability of the nervous centre. At this stage there is less distress but greater danger; that the respiratory centre is depressed by oxygen want is shown by increased rapidity of respiration on the administration of oxygen. Without artificial oxygen supply, cases in this grave stage pass into death by failure of respiration.

(ii) The General Phenomena Characteristic of Oxygen Want.

From the symptoms detailed in the section on pulmonary conditions the conclusion was arrived at that the most conspicuous feature after gas poisoning was oxygen want.

It would be well at the present stage to review briefly the changes in the organism brought about by oxygen want, a subject to which, in recent years, considerable attention has been paid.

When a supply of oxygen to the tissues is inadequate it is clear there must be modifications in the metabolic processes of the body and chemical products appear in the blood which, quantitatively considered, are abnormal.

When the oxygen supply is diminished suddenly and for a comparatively brief interval we have marked effects observable in the nervous centres, both medullary and spinal. There is a primary excitation of the activity of the motor centres, both somatic motor and visceral motor. The result is spasm of the voluntary muscles and vaso-constriction of blood vessels. In the early stages it has been shown that the cardio-inhibitory centre is abnormally sensitive. (*Bainbridge and Dale.*) The greater susceptibility of the medullary centres as compared with the spinal must also be emphasised. Similar results are brought about by CO_2 excess. In the case of the respiratory centre oxygen want has the immediate effect of increasing the susceptibility of the centre to CO_2. As a consequence there is immediate augmentation of the breathing, and unless the discharge of CO_2 is interfered with, a consequent gradual lowering of the CO_2 content of the blood, with a corresponding quieting down of the breathing. The depression of the heart's function, from deficient oxygen supply, may be such as to neutralise the tendency to increased blood pressure early brought about by the action of oxygen lack on the vaso-motor centres.

If the condition of oxygen lack be continuous the increased excitability of the nervous centres diminishes. With very severe oxygen want the respiratory centre begins to fail altogether. It is to be

assumed that when the oxygen supply is inadequate, products of activity arise which poison the various structures and their normal responsiveness to stimulation ceases.

The result is that after prolonged oxygen lack, even though not of great intensity, the nervous centres tend to pass into a condition resembling narcosis. It follows, therefore, that the nervous mechanisms normally controlling the circulation are in a condition of comparative stupor. With respect to the heart the effect of the oxygen want will be gradually to destroy its efficiency, the tone and contracting force are depressed and the heart passes into a state of dilatation.

Later, widespread and manifold degenerative changes can be produced by severe oxygen want in the nervous system, as in other organs. It is well known that carbon monoxide poisoning produces symptoms ranging from acute headache and mild forms of neuritis to multiple sclerosis, paraplegia, hemiplegia, paralysis of groups of muscles or of single muscles, as well as vaso-motor and trophic disturbances. This is explained by many as the consequence of oxygen want.

Further enquiry is needed as to nervous results of gassing found in military cases. Probably many symptoms properly assignable to oxygen want in these cases have been wrongly attributed to shell shock or other causes. In the Air Services medical officers have been slow to recognize that acute headache and other nervous disturbances have been due simply to oxygen want at high altitudes, and not necessarily, if at all, to the mechanical dangers and strain of flying.

(iii) Changes in the Heart and Blood-vessels.

In considering these changes it is desirable to discriminate between the subjects of a sudden intense dose of gas, and those who continuously inhale small quantities. We may call the first group acute cases and describe the second group as chronic cases.

In fatal acute cases of gas poisoning, dying within 24 hours, the heart is usually found distended to a considerable degree with fully clotted blood. This is observed even when the postmortem examination is made within two hours after death. When death occurs later, in about three days, dilatation is usually though not invariably observed. Subepicardial hæmorrhages are sometimes found, and the pericardial cavity may contain bloodstained fluid. At present we have no histological evidence of any myocardial change in such rapid cases.

Early Tachycardia.—Whether fatal or non-fatal we have certain characteristic functional changes in the heart in the early stages of acute cases. Within the first few hours the pulse may sometimes show so extraordinary a degree of rapidity as to be uncountable. This we may call the early tachycardia and it may sometimes be associated perhaps with a condition of shock. But independently of shock evidence is accumulating that such early tachycardia is brought about by an early developing oxygen want. In a number of cases of early tachycardia under observation at Porton a very marked improvement in the heart-beat has resulted from the administration of oxygen.

Diminution in frequency and increase or strength of the pulse is almost the invariable result of oxygen administration after oxygen want has developed.

Nevertheless a considerable number of cases do not show this early tachycardia. The pulse remains slow though it is accelerated by the mildest exercise.

Right-sided Dilatation of Heart.—Amongst other early symptoms there is much more constantly exhibited an acute dilatation of the heart on the right side. It has been observed as soon as seven hours after gassing, but disappeared in 24 hours under oxygen treatment. It is to be further noted that this acute dilatation may be only temporary, disappearing during convalescence.

Accentuation of the second Cardiac Sound.—The clinical evidence of this is well-established. Lately a number of observations on gassed goats at Porton indicate that it is a prominent sign up to about seven hours after gassing, then tends to become less marked, and at 31 hours only about 22 per cent. of animals show it. This sign must presumably be connected primarily with the raised tension in the pulmonary artery and a more vigorous contraction of the right side of the heart.

Tachycardia upon Exercise.—More remote cardiac effects may be observed in the period passing into that of convalescence. Tachycardia has been observed to persist at rest both clinically with man and in the Porton experiments with goats. But independently of the tachycardia at rest there is prominently shown a tachycardia after exercise. This may be exhibited in two ways: the pulse rate may increase more than the normal pulse for a given amount of exercise, or it may return to the normal more slowly after exercise than in the ungassed animal. This tachycardia upon exercise may persist for several weeks. It has further been observed at Porton that this secondary tachycardia is either absent or inconspicuous in cases which were treated early with oxygen, and may be alleviated in men by oxygen administration.

Changes Characteristic of the Period of Convalescence.—Clinical observations (*T. Lewis, Riddell, Price Jones and Hunt*) indicate that temporarily as large a proportion as 36 per cent. of their gassed subjects may exhibit the so-called "*effort-syndrome.*"* There seems no sufficient reason to assume in such subjects a specific change in the tissues of the lungs, which might be held accountable for such a symptom as breathlessness; in some cases, though not in all, there are grounds for believing that in the earlier asphyxial stage the heart may become permanently strained. There is no evidence of a permanent dilatation of the organ, though this point has been carefully investigated. In the various cases admitted into the special hospitals for the heart, gassing is regarded as a relatively unimportant cause, and where it occurs in the histories it is stated that in as many as 30 per cent. the men were at the time of gassing probably already affected with the condition which exhibits the "effort-syndrome." (*T. Lewis.*) The condition, as far as

* "Effort-syndrome" is the name applied to the conditions of D.A.H. or "irritable heart."

gassing is concerned, must be regarded as a feature of convalescence, and not as a persistent state. Recent observations indicate that where the " effort-syndrome " is present the breathing is extremely shallow, and as a consequence abnormally frequent. The Hering-Breuer reflex on increase or diminution of volume of the lung seems to be greatly exaggerated, with consequent great impairment of the efficiency of breathing. (*Haldane and Meakins.*) Though so far but few cases have been available for examination, it is worthy of note that all such cases have shown either a " buffer " deficiency or slight acidosis. (*Barcroft.*)

Functional Changes in Chronic Poisoning.—Though acute cases of gas-poisoning are of not infrequent occurrence in factories, industrial experience furnishes a majority of chronic cases. When the cumulative effect of the poison is such as to incapacitate the subject the clinical symptoms are usually dyspnœa on slight exertion, attacks of giddiness, fainting and cardiac pain, palpitation, and hot and cold flushes. The pulse is usually rapid, weak and irregular, the tachycardia is aggravated by exercise and exertion. After rest the pulse-rate may be abnormally slow and the tension of the pulse low. Dilatation of the heart is shown, associated frequently with asthma, bronchitis and emphysema. (*Shufflebotham.*)

Capillary Hæmorrhages.—It is held by some observers that the coagulability of the blood increases after " gassing." (This point will be more fully discussed later.) Such increase of coagulability is held to account for the formation of small masses of fibrin (and these might also become detached from thrombosed pulmonary vessels), which, passing into the smaller systemic vessels, form emboli. The ring-hæmorrhages which have been described in the brain are believed by some to originate in this manner. (*McNee and Dunn.*) The histological appearances relied upon to support this view are, however, susceptible of other interpretations. (*Shattock, Mott.*) It seems more likely that the minute hæmorrhages observed in the cerebral cortex are not embolic but the result of local capillary thrombosis arising from the damage done to the vessel-walls, probably by oxygen want. The fact that these have not been observed in gassed animals but only in man is possibly due to the peculiar anatomical arrangement of the cortical capillaries found in man. (*Mott.*)

Blood Pressure.—Experimental observations in animals indicate that a fall of blood pressure appears early and is permanent. With strong doses (1 in 2,000 chlorine with cats) the fall may be 50 per cent., its magnitude depending on the concentration. The initial fall may be preceded by a temporary rise, and it occurs before there are distinct signs of lung œdema or an asphyxial state of the blood. The blood pressure may be restored to normal by intra-venous injections of gum-saline, less effectively by pure saline. The subsequent onset of œdema is not prevented or even delayed by such injections. (*Bayliss.*) This fall of blood-pressure is not temporary but is still observable twenty-four hours after the gassing, should the animals survive. (*Barcroft.*)

It is possible that this fall of pressure may be connected with an early disorganisation of the respiratory surface. Some thickening of

the alveolar walls, due to œdema perhaps of the substance of the wall, interferes with respiratory exchange, and presumably an early condition of oxygen want is established which reacts in the ordinary way on the efficiency of the medullary and spinal centres. Further the altered activity of the heart is an additional factor in the phenomenon. An alternative explanation is that as the result of considerable dilatation of the pulmonary vessels there is accumulation and stasis of blood in the pulmonary vessels, *i.e.*, the animal has a large quantity of blood withdrawn from the systemic circulation into the lungs. There is experimental evidence that no large withdrawal of blood into the splanchnic area occurs. (*Bayliss.*)

(iv) Changes in the Mouth, Larynx, &c.

(*a*) In fatal cases of irritant gas-poisoning hæmorrhage of the gums is often found, and the mucous membrane of the larynx is nearly always intensely congested. The lining of the trachea may also be congested and the trachea may be full of frothy liquid.

There may be some redness of the œsophagus.

(*b*) In non-fatal cases workers in such gases have been found to suffer from hæmorrhage of the gums and pyorrhœa alveolaris, and this trouble is attributed to the employment.

With some forms of irritant gas, *e.g.*, dichlorethylsulphide, varying degrees of congestion of the mouth, fauces, pharynx and larynx are found. These may, in severe cases, culminate in acute pharyngitis and laryngitis, there being much difficulty in swallowing even liquids. Later erosion of the mucous membrane and finally its separation in large sloughs may occur. The œsophagus is not usually affected, but the trachea is even more rapidly involved in the necrotic change than the upper air passages.

(v) Changes in the Stomach and Bowels (human).

(*a*) In fatal cases well-marked gastritis may occur. P.M., a catarrhal condition of the mucous membrane is often found with or without submucous hæmorrhages.

(*b*) In non-fatal cases gastritis is one of the commonest results of gas poisoning, and even after treatment a chronic form of dyspepsia often ensues, and may persist for many months. This gastritis is particularly the case after dichlorethylsulphide, and is prominent also in animal experiments.

Hæmatemesis occurs in some instances.

Diarrhœa with stools containing blood and mucus is often found in cases of gas-poisoning, and experimentally the same has been observed in animals.

(vi) Renal Changes.

In factories again it has been found that :—

(*a*) In fatal cases varying degrees of congestion of the kidneys are apparent post-mortem, and in some cases there is venous engorgement

(*b*) In non-fatal cases albuminuria is frequently found as a result of chloropicrin poisoning.

Nephritis in chlorine poisoning has been observed but so rarely as to make it uncertain whether or no it was accidental. Congestion of the kidney was the rule. (*Elliott*, 1915.) With man and animals killed with chloropicrin and phosgene well marked nephritis is not uncommon. (*Porton experiments.*)

(vii) Changes in the Blood.

Concentration of Blood.—The chief factor in producing the concentration of the blood which is observed after gas-poisoning is—

(*a*) The production of pulmonary œdema.

Other contributory factors may be—

(*b*) The incidence of shock.

(*c*) The partial asphyxiation of muscular and other tissues enhancing the local lymph production.

It may be that any loss to the plasma such as is involved in the production of œdema of the lungs would be made good by reabsorption of fluid from the tissues. But according to recent views ("*Memorandum upon surgical Shock*"—*Medical Research Committee*), it is possible that one of the factors of the condition of shock is a loss of capillary tone and a stagnation of blood in slack capillary channels. The slowness of the capillary circulation through the muscles and other tissues needing a plentiful supply of oxygen will lead to defective oxidation, thence to acidosis and further to a tendency for passage of water by osmosis from the blood. Under these circumstances the machinery for making good the loss in the lungs will be out of gear, and the concentration of blood produced in the lungs will persist, and may even be intensified, by the events taking place in other tissues.

Experiments in rabbits (and observations on man) indicate that some hours after gassing a large increase in the number of red corpuscles is observable. This is considered as mainly the consequence of plasma removal, and may be spoken of as an acute *relative polycythæmia*, due to concentration. Though not to be explained as the consequence of the production of pulmonary œdema alone, there appears to be a rough relationship between the degree of œdema and the intensity of the oligæmia* in rabbits. (*Barcroft and Dufton.*)

Absolute Polycythæmia.—Independently of the early temporary relative polycythæmia, there occurs both in man (*Price-Jones and Hunt*) and in animals a *true absolute* polycythæmia. This may be due either to oxygen want or excess of CO_2. It is worthy of note, however, that in animals gassed one to four months previously, this chronic polycythæmia can be temporarily removed by two or three days' exposure to a high oxygen tension in the oxygen chamber. Generally

* By the term *oligæmia* is understood a reduction of the total bulk of the blood, whether accompanied or not by a reduction of the corpuscles. If the corpuscles increase in number in a sample of blood within a period during which it is improbable that they can have been added to the circulating blood, a reduction of blood volume may be inferred

it may be regarded as the usual compensatory adjustment following chronic oxygen deficiency. (*Barcroft and Dufton.*)

Leucocytosis.—A general leucocytosis is accepted as the usual result of asphyxiant gas poisoning, and this appears within a few hours after exposure.

In man a delayed leucocytosis has been described, in which the lymphocytes are the prominent cells, their percentage numbers approximating to those of the polymorphs. It is stated that this lymphocytosis may be of importance in testing the truth of a previous history of gassing within the past twelve months. This condition may develop after a month and persist for eighteen months. (*J. Miller.*)

Coagulation Time.—Clinical observations are somewhat discordant upon this point. It is said that in the early stages of gas-poisoning there is a considerable diminution in coagulation time. (*McNee and Dunn.*) German observers also maintain that this is the case during the acute phase of the poisoned state. On the other hand French observers have been unable to confirm it. Experiments on animals again tend to oppose the view. With cats and dogs it has been found that the coagulation time, if altered, is increased rather than diminished. (*Bainbridge and Dale.*)

Acidosis.—This condition is fundamentally associated with oxygen want. It may be insisted that its appearance in gassed subjects is primarily due to this oxygen want, and the principles of treatment should be founded not on the neutralisation of the acid tendency of the blood but upon restoring the oxygen supply to the tissues.

In experiments on gassed animals it has been shown that this acidosis is a prominent feature, and that it is increased in degree by exercise. (*Barcroft.*)

In a number of cases in the Base hospitals it has been shown that gas poisoning in man leads to a condition of slight acidosis. (*Barcroft.*)

(B).—CONSIDERATIONS INFLUENCING TREATMENT.

The possible factors which contribute to the conditions already described are :—

(i) The direct damage done to the respiratory apparatus and pulmonary blood-vessels, resulting in deficient respiratory exchange.

(ii) Absorption of the actual gases inhaled or primary products of disorganised lung tissue.

(iii) Absorption by the blood of toxic substances secondarily produced in the lung or elsewhere.

(iv) Shock, however produced.

As regards (ii) it has been observed that the intravenous injection of serum taken from cats killed with chlorine causes only a slight and transitory fall of blood pressure. A mixture of normal defibrinated blood and Ringer's solution, or Ringer's solution alone containing free chlorine if injected produces no effect. (*Bayliss.*) Neither the injection of phosgene intravenously (*Douglas*) or of chloropicrin subcutaneously (*Peters*) has produced any obvious effects. In the case of

dichlorethylsulphide there is evidence that when the substance is injected hypodermically, or, in the case of rats, absorbed through the skin, it produces the characteristic bronchitis, conjunctivitis, &c. This substance may therefore produce part of its effects through being circulated in the blood. (*Haldane, Carleton.*) In man also, after the primary erythema has largely disappeared, fresh patches of erythema may develop about ten days after the exposure, though every care has been taken to prevent infection by clothes, &c. (*Barcroft.*)

In order to obtain evidence as to whether toxic compounds were directly produced in the lung by the action of *irritant* gases, the lung-substance of animals killed with chlorine and phosgene has been ground up and extracted with Ringer's solution. It is found that such extracts are harmless whether injected intra-peritoneally or subcutaneously. (*L. Hill.*)

If the blood or tissue œdema taken from a guinea-pig killed with phosgene be injected into a second animal no results are found. Serum, through which phosgene has been bubbled, may be injected without harm into guinea-pigs. By arranging a double air supply to the lungs and leading the irritant gas to one lung only, the evidence is that that particular lung alone is affected, the other lung remaining sound and sufficing for the general requirements of gaseous exchange. It has further been shown that phosgene apparently has no influence on the heart. (*L. Hill.*)

Sulphuretted hydrogen need not be considered here as it has only a quite minor importance as a pulmonary irritant.

It cannot be stated, with certainty, that *all* the effects these irritant gases produce are secondary to deficient respiration. Nevertheless, at present we have no evidence that the manifold signs and symptoms they produce within the body cannot be fully accounted for by reference simply to such deficient respiration and, in particular, to oxygen want.

As regards (iii) at present we have no definite information.

With respect to (iv) in the earliest stages it has been suggested that the symptoms of shock are not uncommon. A rapid thready pulse, sometimes uncountable and, generally, the signs of collapse, are not infrequent. But the cause of this collapse is not yet apparent. At present we can only connect it with afferent impulses from the damaged lungs. An analogy might be drawn from the condition of shock brought about after a severe burn. On the other hand it is possible that all the symptoms may be due to anoxæmia.

(1) Fundamental Principles in Treatment.

We may found our rules of treatment for irritant gases upon the hypothesis that the all-important factor producing the poisoned condition is mainly (i) the direct damage occurring to the respiratory apparatus and resulting in deficient respiratory exchange.

The principle underlying these rules depends upon the necessity of diminishing normal metabolic activity as far as possible, and at the same time, when the conditions require it, supplying oxygen, which

the damaged lung may be unable to absorb to the necessary degree from atmospheric air. The three cardinal points in treatment are: (*a*) Rest, (*b*) Warmth, and (*c*) Administration of oxygen.

(*a*) *Rest.*—The first essential of sound treatment must be to secure the most complete *bodily rest* possible, in order to reduce tissue (especially muscular) respiration in the body and the demand for oxygen. Moreover, muscular movement involves a rise of systemic blood pressure; this leads to a rise of pulmonary pressure, and so promotes the production of œdema. The question whether simple rest should be aided by giving narcotics is a matter on which there is much difference of opinion. Small doses of chloral may be useful, but morphine is inadvisable unless restlessness and fright are out of all proportion to the disturbance of respiration. Morphine is generally undesirable since it has a specific depressant action on the respiratory centre; chloral does not show this.

(*b*) *Warmth.*—Considerable stress must be laid upon the desirability of keeping the patient warm, whether signs of collapse are present or not. Clothes saturated with the gas will have to be removed, but adequate covering must be substituted. If the clothes were not removed they might continue to give off the gas they had absorbed. In a cold atmosphere animals, especially small animals, suffer a great increase of metabolic activity in order to maintain their temperatures. Though this may not be equally the case in man, it must be remembered that shivering, if it occur, means considerable carbonic acid production and oxygen demand, and further, implies a rise of blood-pressure. Moreover, there should be *still* air, *i.e.*, an absence of draughts, if the metabolism is to be lowered to the utmost.

(*c*) *Administration of Oxygen.*—It may first be pointed out that experience with animals abundantly supports the value of such treatment. With different species of animals it has been observed that the only treatment, so far tried, that relieves the symptoms after "gassing" and subsequent œdema is inhalation of oxygen. (*L. Hill, Barcroft, Bayliss.*)

In the early days of gas poisoning the value of supplying oxygen in man was disputed by some. This was frequently because (1) the oxygen was not properly given and was not actually inhaled, and (2) it failed to afford relief to the extremely severe asphyxial cases with marked flooding of the lungs on the one hand, and in the milder cases in which there was no oxygen want but much dyspnœa on the other. In some intermediate cases, observers may also have been misled as to its beneficent effect by the increase of respiration following oxygen supply, due to the restoration of the respiratory centre to its normal irritability.

The administration of oxygen is only desirable in cases which present obvious signs of oxygen want. (*See the quotation from Haldane above, p.* 6.)

The guiding principles in the oxygen administration must be, first, that it must be so given as not to increase the amount of carbonic acid round the patient's mouth and nose; and, secondly, if it is to be administered continuously in conditions where transport is difficult, it

must not be wasted. The dead space in the mask should therefore be as small as possible. This is particularly important when the breathing is shallow. In such cases it may be preferable to use a nasal tube rather than a face-piece, although a proper face-piece arrangement is more economical of oxygen. The oxygen should be administered continuously, or nearly continuously, and with this in view it should be delivered as economically as possible.

(*a*) *Bleeding.*—Clinical opinion must be regarded as holding this of high value. As routine treatment in *all* cases we are disposed to question the desirability of its employment. We think it can only be held to be scientifically sound when there are obvious signs of distension on the right side of the heart. It is justifiable in the condition of acute dyspnœa with "blue" face and venous congestion. Frequently the benefit is transitory. It should be carried out slowly and from 15 to 20 minutes should elapse during the bleeding, the quantity removed should amount to about 20 ounces (about 550 c.cm.).

In those cases which show no signs of venous congestion we have no hesitation in condemning it entirely. We consider it is unjustifiable in a "grey" case.

Animal experiments supply no evidence that bleeding has any obvious effect in delaying the onset of severe symptoms and death after chlorine poisoning. If performed after the development of pulmonary œdema it may result in rapid failure of the heart and death. Frequently the severity of the asphyxial symptoms is increased. (*Bayliss.*) It should be mentioned, however, that in a large number of experiments on goats at Porton, bleeding was only observed to produce heart-failure when there was much struggling.

(*b*) *Intravenous Injection.*—The advocacy of anticoagulant injections seems to have been based on a complete misconception, since it is not definitely established that the coagulability of the blood, as such, is altered. Intravenous injections have been employed with the view of diminishing the concentration of the blood, in other words, restoring the liquid that has been lost, largely in the production of the pulmonary œdema. It must first be pointed out that considerable injections of saline tends to produce pulmonary œdema even in the normal animal. If injections in quantity are employed it is only permissible to make use of a dilute gum-saline, such as a solution of 2—5 per cent. gum in Ringer's fluid. But it is clear that unless any leakage from the lung capillaries can be stopped, intravenous injections may do more harm than good.

(*c*) *Administration of Alkalies.*—The administration of drugs, such as sodium lactate, sodium bicarbonate, urea, and ammonium citrate has been employed with the object of combating the acidosis of the blood. It may first be asked whether it is desirable, even if possible, to remove this acidosis by the administration of alkali or of some substance which will yield alkali in the body. We must regard the acidosis as a physiological reaction to the onset of oxygen want, tending to promote increased oxygen intake by augmenting the activity of the respiratory centre. The hyperpnœa which develops therefore may be positively beneficial, and should certainly not be regarded necessarily

as a symptom to be abated. The fundamental treatment must aim at relieving the condition of oxygen want by administration of oxygen. If, for any reason, it is essential to directly combat the acidosis, it must be pointed out that alkalies or substances producing alkali in the body are only effective if given in large quantities and repeatedly, as, for instance, sodium bicarbonate in doses of 60 grains every four hours. The attempt to neutralise the acidosis by drugs alone is unjustifiable interference with the natural machinery for securing an increased oxygen intake.

(*d*) *Bronchial Spasm.*—This may be present in cases of chlorine poisoning. With the idea of relieving the condition atropine has been employed. We consider that the use of atropine should be discouraged, in the first place because the evidence preponderates against its value, and in the second place because it tends to increase the activity of the heart and unnecessarily use up its reserve energy.

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MEDICAL RESEARCH COMMITTEE.

+ Special Report Series

REPORTS

OF THE

CHEMICAL WARFARE MEDICAL COMMITTEE.

No. 2. THE HISTOLOGICAL EFFECTS PRODUCED BY GAS POISONING AND THEIR SIGNIFICANCE.

APRIL, 1918.

In January, 1918, the Director-General, Army Medical Service, with the concurrence of the Controller of Chemical Warfare, appointed the following Committee to prepare reports, based upon information received from all sources at the Chemical Warfare Department, for submission to him with a view to their distribution to those concerned, to make suggestions for further co-ordinated medical investigations that may seem desirable, and to advise him generally in respect of the scientific medical aspects of Chemical Warfare :—

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REPORT ALREADY PUBLISHED.

No. 1. Notes on the Pathology and Treatment of the effects of Pulmonary Irritant Gases.

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THE HISTOLOGICAL EFFECTS PRODUCED BY GAS POISONING AND THEIR SIGNIFICANCE.

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I.—THE EARLY CHANGES PRODUCED IN THE LUNGS BY GAS POISONING, AND THEIR SIGNIFICANCE.

By J. S. Edkins and N. Tweedy.

(*From the Physiological Laboratory of Bedford College.*)

Methods.

The standard method we have employed is fixation in formalin and corrosive sublimate in the distended state, completion of hardening in absolute alcohol, sectioning in paraffin, and staining in Ehrlich's hæmatoxylin and Biebrich scarlet.

In nearly all cases sections have also been examined after staining in

(1) Weigert's elastic stain and lithium carmine.
(2) Mallory's stain.
(3) Weigert's fibrin stain.
(4) Pappenheim's methyl green and pyronin stain.

Various microchemical methods have also been employed.

The Histological Appearance of the Normal Lung of the Rabbit.

In the rabbit there is an absence of any obvious lobular arrangement. The smaller bronchial tubes pass into atria practically directly, the cubical epithelium flattening out, and the appearance of a regular row of cubical cells being lost. In the alveolar walls many nuclei are seen, their appearance varying according to whether the view is side-face or full-face. An alveolar wall viewed full-face shows nuclei roughly circular but frequently irregular and staining lightly. Viewed in profile the nuclei appear much denser, and are generally elliptical. The more stretched the alveolar wall, the more flattened the nuclei appear. These nuclei may be regarded as belonging to several systems, the more irregular being probably nuclei of connective tissue cells in the walls, the rounder mainly nuclei of the epithelium. Except for the nuclei it is difficult to define the flattened respiratory epithelium in profile view in ordinary specimens, it is perhaps most easy in Mallory-stained sections. The difference in form in the nuclei is best demonstrated in lithium carmine specimens.

The different cells in the blood of the rabbit are easily recognised in standard specimens, the polymorphs (pseudo-eosinophils) retaining their granules, which exhibit a crimson-red colour with Biebrich scarlet, true eosinophils taking on a more orange-scarlet. The granules in polymorphs are small and spherical and in eosinophils they are larger and ellipsoidal.

It is not uncommon to find in small veins apparent dilatations in which are seen collections of polymorphs. In the lungs which we have examined and which show no other sign of abnormality, these are found sufficiently frequently to suggest that they may be a feature of the normal lung.

Lymphatics are only easily recognised when somewhat distended. They are exhibited in the œdematous lung plentifully around the arteries (Figs. 1 and 2), and afferent vessels can be seen opening into these periarterial lymphatics passing into alveolar walls (Fig. 3). Except when of large size the veins and bronchi do not exhibit any conspicuous lymphatic vessels. The subpleural lymphatics are not well marked in the œdematous lung of the rabbit. The appearance of the œdematous lung clearly indicates that the normal channels of drainage for the alveoli are by periarterial lymphatic vessels. We regard the rabbit's lung as favourably adapted for studying the changes in the lymphatic system in various conditions and the influence that gassing brings to bear upon cell invasions in the lung tissues.

The Significance of Lymph Formation in the Lung.

The Normal Production.—It has to be remembered that under ordinary circumstances water is constantly being evaporated from the alveolar walls into the alveolar air. This must result in a concentration of the tissue fluid in and on the walls which further tends to promote the passage of water outwards from the capillaries. This is probably controlled by a flushing mechanism, which is presumably one of some vigour. We may assume therefore that there is proceeding continuously a comparatively vigorous production and drainage of lymph from the alveolar wall. There is, in other words, always a tendency to pulmonary œdema, but the balance between production and drainage is such that no accumulation of liquid occurs. Clinical and experimental observation shows that the production is closely associated with pulmonary blood pressure.

We must further remember that the alveolar epithelium must be regarded as an external tissue exposed to atmospheric air with the various noxious substances it may contain. Substances which bring about irritation of the pulmonary epithelium by chemical or mechanical agencies may obtain ingress into the air sacs, and micro-organisms will obtain easier access than to the internal tissues. Some restraint over the activities of these foreign agents may be exercised by the lining membrane of the air passages; but it seems necessary to postulate the existence of a very highly developed defensive mechanism in the air sacs as compared with most structures of the body. Finally, a lymph supply to the alveoli is essential for the maintenance and repair of the lung tissue, in respect of the requirements of its living state, as is the case in all other living tissues of the body.

We must therefore regard normal lymph production in the lung as directed, in the first place, to promoting the healthy condition of the pulmonary tissues, exposed as they are to ready assault from without, and secondly to the provision of the water which is evaporated from the alveolar walls.

The Alveolar Œdema resulting from the Action of Irritant Gases.

As a consequence of the advent of irritant gases into the alveolar air, alveolar œdema usually appears. This may result from different main causes :—

(1) It may be simply a response of increased lymph production to some appropriate local stimulation.

(2) It may be the result of damage to the alveolar epithelium and the capillary walls, such that increased permeability occurs as far as the plasma and its constituents are concerned, though not permitting diapedesis of erythrocytes. In severe poisoning, however, this may even occur.

(3) The damage done to the alveolar walls may lead to the formation of new chemical substances which osmotically induce a passage of water from the capillaries. It is perhaps even possible that the irritant substances themselves or their chemical products may be of minor importance in this respect.

(4) It may be the result of such disorganisation of the walls of the vessels or spaces containing lymph that a definite leakage is established.

On the other hand, the accumulation may be the result of defective drainage, the augmentation of drainage may not be of the same degree as the exaltation of production. It may even be that the activity of the drainage mechanism is partially suspended. It is possible that such a reaction has become evolved in order, when necessary, to bathe more extensively damaged pulmonary tissue with healthy lymph. In some way or other the balance between production and normal drainage is upset, and consequently œdema occurs. There may only be a slight difference to the advantage of production and then œdema slowly develops. The increased production may not persist, and later the activity of the drainage mechanism may overtake the accumulation, and after a short time the œdema may be removed ; or it may happen that when the œdema is primarily due to leakage from defective walls, this defect may not be immediately, but only gradually, developed ; œdema therefore would only appear after a latent period.

Any rise in pulmonary blood pressure tends to promote pulmonary lymph production. Whatever causes bring about a rise of systemic blood pressure, such as muscular activity, these also influence pulmonary blood pressure. Œdema then may not develop except as the result of muscular exertion.

From the appearances presented in histological specimens of lungs examined at different intervals after gassing there is little evidence of suspension of activity of the drainage mechanism. The periarterial lymphatics, normally hardly obvious, gradually increase in size by the distension they suffer from their engorgement with lymph. They may, in extreme cases, form a ring of swollen vessels of width equal to or greater than the thickness of the muscular coat (Fig. 2). There seems little reason to regard this distension as due to any obstruction of the

outward flow of the lymph from the lungs; it is therefore justifiable to connect it with the vigour of production.

We are therefore led to the view that the œdema is the consequence of excessive lymph production, and that this production is the adapted response which the lung tissue makes to the stimulus afforded by the irritant gas or the changes in the tissues such irritant gases immediately induce. The accumulation, though its advantage in maintaining or restoring the lung tissues may be great, has the disadvantage that it may fatally interfere with the gaseous exchange. However necessary its appearance may be to combat the poison, when in excess it is as desirable to get rid of it as in the case of pus in an abscess. Our means for doing this are limited. The activity of the drainage system may become exalted and thus a natural elimination occurs. It seems, however, that some gain might perhaps be obtained if, when possible, posture were adapted to assist in its removal by inviting the accumulated liquid to pass away by the air channels. This has the disadvantage that the comparatively sound areas of the lung might be temporarily blocked by the liquid. But there may be cases in which a fatal result is certain from oxygen-starvation and its attendant evils in spite of oxygen inhalations, and it is possible that in these cases removal of the accumulated liquid by posture, if posture could effect it, might be the only method of avoiding death.

The Histological Changes in the Gassed Lungs.

Condition of the Lung one hour after Gassing with a Minimal Lethal Dose.—No alveolar œdema is found (Fig. 4) and under low magnification there is little to distinguish it from normal. The veins, large and small, are somewhat more turgid with blood. The arteries are not distended.

As regards the lymphatics, there is evidence of slight distension of the periarterial (Fig. 5), probably more than exists in the normal lung, and at places where the afferent lymphatic vessels open into the periarterial there are seen small mononuclear cells in some quantity. (Fig. 3).*

With respect to the alveolar wall, there is no marked difference from the normal. The rounder nuclei are slightly more numerous, but this may possibly be the result of more distended blood capillaries and lymphocytes therein. In the wall there are certainly more polymorphs, but these are intravascular and generally of compact form. The granules therein are massed together but quite distinct. Eosinophils are not numerous. When an alveolar wall is viewed full-face, the polymorphs vary from about one to four (averaging about 2). There seems to be no proliferation of alveolar epithelium. It is difficult to say definitely whether the alveolar septa are thickened, there seems to be on the whole some thickening, a greater tendency to a vaguer outline in profile of the epithelial covering; sometimes the nuclei are

* A majority of these are probably lymphocytes, but when stained by Pappenheim's method, many of them show the cytoplasm crowded with pyronin staining granules. They may perhaps be plasma-cells washed out of lymph channels.

separated by a marginal band from the air space, which we take to indicate some abnormal thickening. In judging the character of the clearness of the edge of the alveolar wall, we have, of course, only regarded those walls which are cut orthogonally.

There seem to be no changes in the bronchial mucous membrane.

Summing up then the changes which are observable at the expiration of an hour after gassing in the rabbit, we may state that there is no obvious alveolar œdema, the periarterial lymphatics are slightly more distended than normally, the veins and capillaries are somewhat engorged, polymorphs are more numerous though still located in the vessels, lymphocytes are possibly more numerous, and there is no obvious change in the bronchial epithelium. Any tendency to alveolar œdema is balanced by increased activity of the drainage mechanism. The animals were exposed to a minimal lethal dose of gas for twenty minutes, such as might be expected to be fatal in 20-24 hours.

Condition of the Lung 2 hours after Gassing with a Minimal Lethal Dose.—Alveolar œdema is seen at this stage, sometimes in solitary air sacs, sometimes in groupings. It may at places largely fill the air sacs, occasionally it merely forms a meniscus at the side of the alveolus. All degrees of œdema formation are seen, though no alveoli can be regarded as maximally distended (Fig. 6).

Though in some places erythrocytes are seen in the œdema, it must be regarded generally as cell-free.

The arteries are not markedly distended, but the veins and in particular the capillaries show marked dilation as compared with the lung one hour after gassing.

The periarterial lymphatics are very evident, being distended with liquid which resembles in staining affinities the œdema of the alveoli. It is justifiable to regard this as œdema drained off from the alveoli (Fig. 7).

A somewhat striking feature of the peripheral vacuolation of the œdema both in the alveoli and lymphatics (Cp. Fig. 17). The shape of the vacuoles forbids this being regarded as the effect of the histological reagents in causing shrinkage. But it is exhibited not merely by the œdema, but also by the blood in the veins and arteries. We thought at first that this might be regarded as evidence of a positive secretion of gas from the alveolar walls. Its universality in vessels containing fluid in the gassed lung negatives such an explanation. We suggest that owing to the defective gaseous exchange the liquids, plasma, lymph and œdema, become so overcharged with carbonic acid that the physical conditions involved in contact with the walls are sufficient to determine partially its exit.

The bronchial tubes may show considerable proliferation of the cells of the mucous membrane. Amongst those of the lining are many with much segmented and deeply-stained nuclei, independently of the polymorphs which are found invading the mucous coat at places.

In the alveolar walls the capillaries are much distended and many polymorphs are seen. These are sometimes irregular in shape, due to adaptation to capillary channels, but the granules are compact. They appear generally to be located in the vessels.

The alveolar walls are somewhat thickened and some proliferation

of the epithelium is indicated. From the free surface of the epithelium mononuclear cells bud off, which at first are small, with nucleus and cytoplasm staining fairly deeply with appropriate dyes. Later these cells become much larger, the cytoplasm and nucleus both stain but lightly, and they exhibit phagocytic power. They may in some cases be visible in fair number as early as the second hour (they are not entirely absent in the normal lung), but they seem to reach a maximum at about the second or third day. They quite early show particles of brownish or black substance in their cytoplasm, which we believe to be frequently broken down blood pigment. In some cases it is simply carbon.

Condition of Lung of Rabbit 5½ hours after Gassing with a Sub-lethal Dose.—A lung in this condition is selected for contrast with that at two hours after lethal gassing, as it may be regarded as presenting changes less intense and culminating perhaps less rapidly.

Vascular congestion, though considerable, is less marked than in the 2-hour case, the arteries are not markedly distended with blood.

Alveolar œdema is almost insignificant, it is recognisable in a few alveoli only.

The bronchial tubes show disorganised epithelium, which is seen proliferating, and there is some invasion of polymorphs. These are more numerous than normally in the submucous coat. Some of the cells at the border of the mucous membrane show segmenting nuclei.

The edges of the septa separating the alveoli are somewhat swollen and generally fail in sharp definition. Menisci of œdema are seen in many places along side the alveolar walls. Proliferating epithelial cells in the alveoli are practically absent.

The periarterial lymphatics are markedly distended, apparently out of proportion to the amount of œdema found in the alveoli (Fig. 8).

Polymorphs are numerous in the alveolar walls. They are mainly intravascular. They may be irregular in shape, adapting to the capillary channels, but are not swollen and may be regarded generally as compact in respect of granular content. Many small vessels are crowded with polymorphs.

Eosinophils are not conspicuous.

The outstanding features of the specimen taken as example were the presence of large numbers of polymorphs and the disorganisation of the bronchial epithelium (neither of which characters are well marked at earlier periods). We take this as representing a type of lung condition in which the production of lung œdema has been suppressed by the activity of the drainage mechanism in over-coming the increased production, and thus no accumulation has occurred. There is, however, the possibility that some œdema did exist earlier, and that the drainage has overtaken the production, removing any accumulated liquid.

Condition at 24 hours after a Sub-lethal Dose of High Concentration.—The appearance of the lung tissues at 24 hours after gassing depends primarily on the strength of the dose of gas. If sub-lethal, but nevertheless of considerable concentration, and the animal be killed at the end of 24 hours, the changes in the lung are sometimes difficult to precisely interpret, since the condition may be one in which progressive changes have advanced somewhat slowly and to a degree not very

intense, or on the other hand the maximal changes may have been passed and a process of restoration of structure may be already instituted. As regards the œdema, for instance, it may be that it has slowly progressed to the degree found or has earlier been more marked and is in process of being absorbed. It seems to us doubtful if any appreciable advance in direction of repair could have taken place with strong sub-lethal doses of high concentration in 24 hours, and we regard the lung under these circumstances as furnishing an example of a stage in the progressive changes in the disorganisation caused by the poison.

The condition of the lung then after gassing with a sublethal dose of high concentration is as follows :—

The œdema is not great, large areas of lung tissue may be found free from it. Sections may be cut through the lung at places which practically show no œdema (Fig. 9). In other places, however, a fair amount of œdema may be shown, patchy in distribution and not maximal as regards the distension it brings about (Fig. 10).

The bronchial tubes show disorganised epithelium, and in places this is infiltrated with polymorphs. Sometimes the surface material is shed as a lamina of massed cells and mucus. Œdema is visible in some bronchi ; this is to be regarded as forced from the alveoli. In the outer walls of the bronchi eosinophils may be comparatively common, and they may also be present in the lymphoid masses. Where the alveoli are clear of œdema the periarterial lymphatics are not obviously distended. Where there is much œdema the lymphatics are also found distended (Fig. 10).

Polymorphs are very numerous both within and without the blood vessels. Their nuclei in many cases stain extremely deeply, and are segmented frequently into six or more rounded masses. The granules are distinct, but show a tendency to become less compact. In some cases the polymorphs appear swollen, with granules diffusely spread.

Eosinophils are more common than in earlier stages ; they do not as a rule show any tendency to undergo the changes the polymorphs exhibit.

A well-marked feature now is the presence of free alveolar epithelial cells. These cells display phagocytosis. They may sometimes be seen actually budding, at other times lying adjacent to, but disconnected from, the epithelium in the peripheral part of the œdema against the alveolar wall. When recently budded these macrophages are generally ellipsoidal, a longer axis of about 12μ, a shorter of about 8μ. They rapidly enlarge to 18-20μ in the long axis. The nucleus is comparatively dense, and stains deeply in early stages. It becomes much larger, shows one or two well-marked nucleoli, and stains less deeply as the cell enlarges. The phagocytic power is displayed quite early, the cells ingested being red blood corpuscles and polymorphs. The result of the intracellular digestion of these cells leads to a residue of dark granular matter appearing within the more mature cells which resembles carbon particles. These epithelial cells, which are frequently conspicuous in lungs of different animals, are presumably the agents by which foreign or dead solid material is removed from the cavity of the alveolus or the alveolar walls.

Condition at 24 hours after a Lethal Dose.—The most striking feature of the lung after death in 24 hours is the widely spread flooding of the alveoli with the œdema fluid. (Figs. 11 and 13.)

The periarterial lymphatics are widely distended (see Fig. 12, Rabbit XIX). There is evidence of acute emphysema, many large spaces being seen formed by the confluence of ruptured alveoli.

Hyperæmia is marked, arteries, veins and capillaries all being distended. Occasionally, but infrequently, there is evidence of collapse, an œdematous area being constituted of confluent alveoli filled with fluid, interspersed amongst areas made up of collapsed alveoli (Fig. 14).

The bronchial tubes frequently contain œdema liquid, consequently the passage of air is seriously interfered with though the alveoli may not themselves be markedly flooded. At this stage also it is observed that the bronchial mucosa is invariably disorganised, much proliferation of the epithelium being shown, but this is not shed to any marked extent. Polymorphs invade the epithelial layer in large numbers.

The alveolar walls are thickened. A considerable number of macrophages may be seen, sometimes containing a little pigment. The polymorphs are seldom compact; usually when in the capillaries they are very irregular, swollen, and the cell granules are diffusely spread. They may invade the œdema liquid; they then take on a more spherical form, though still somewhat irregular. They appear to gradually lose their granules, and at the same time the nucleus fades as regards staining depth, the surface of the nucleus remaining darkly stained for a time, later the whole nucleus becomes evanescent. The different lobes of the nucleus remain connected, and in many cases the whole nuclear mass swells and gradually becomes indefinite. The granules in the meantime seem to diminish in number. It is noteworthy that when these polymorphs penetrate the œdema liquid and are abundant, the œdema may show much fibrin. Ghosts of these extravascular polymorphs are recognisable, in which the boundaries of the cell are ill-defined, the granules still being present, but in which the nucleus cannot be seen. There may also be observed small cell fragments in which a small number of granules persist.

We regard the appearances shown in these specimens taken from animals which died in 24 hours after a lethal dose of gas as susceptible of the following explanations :—

The irritation of the gas induces certain changes in the alveoli and air passages similar to those constituting inflammation, and these are manifested in the intense hyperæmia, the polymorph leucocytosis, the active lymph production, and the changes in the epithelium both of the bronchial tubes and the alveoli.

What precise function is subserved by the polymorphic invasion is somewhat difficult to define. It has no relation to activity of micro-organisms at this stage. The lungs have been repeatedly examined for presence of micro-organisms, and we have never found any infective organisms to account for the changes.* Some chemiotactic influence

* Our thanks are due to Dr. J. A. H. Brincker for investigating many of the lungs with the object of ascertaining presence of micro-organisms.

is apparently exerted by the stimulus of the poison or the changes it immediately brings about, and this attracts the polymorphs to the seat of damage. That they appear to have some influence in the direction of reaction to the change is suggested by the observation that occasionally when animals have died from what is usually a sub-lethal dose we have found that the polymorphic reaction markedly failed in reaching its ordinary intensity (Rabbit XLVII).

Assuming then that the reaction is adapted to some end and not an accidental part of some general pulmonary reaction specially evolved to combat micro-organic invasion and called into operation by any sufficiently intense stimulus, we may regard it as playing a part in coping with the disorganisation brought about by an irritant gas either (*a*) by direct neutralisation of the noxious chemical substances, or (*b*) by assisting in the flushing with lymph of the disorganised surface by promoting its more rapid absorption through the natural drainage channels, or (*c*) by helping in the elimination of damaged tissue by taking a part in its digestion extracellularly, or (*d*) by ingesting damaged tissue, sometimes to the destruction of the polymorphs themselves. It is easy to be assured that the polymorphs become greatly swollen and that their granules diminish. This seems to be followed not infrequently by the breaking down of the cell itself. This, however, is less often the case in air channels where the polymorphs collect after transit through the mucous membrane and presumably become pus-cells, and though somewhat ill-defined preserve generally something of their normal appearance.

With respect to the lymph production, as before stated we must regard this as enhanced and the accumulation in the alveoli as in part due to drainage being incommensurate with formation. We see in these fatal cases after 24 hours a very intense activity of the drainage mechanism but one ineffective in coping with the production. As long as production continues at the same rate the accumulation will not merely persist but increase.

Condition of the Lung after a Sub-lethal Dose which has been followed by Death as the Result of Exercise.—The sections of lung (Figs. 15 and 16) is taken from an animal (Rabbit VIII), which was gassed with a sub-lethal dose of an irritant gas and which we should have expected to survive under ordinary conditions. The animal was subjected to intermittent but rather severe exercise during a period of one hour, at the end of which it collapsed and died. The lung shows practically maximal œdema, and the œdema is present in many of the bronchial tubes. The mucous membrane of the tubes is not greatly affected. In general this shows the ordinary appearance of an animal exposed to an intense but sub-lethal dose of gas, to which is added more marked œdema. A striking difference, however, is the frequent absence of lymph from the periarterial lymphatics which are comparatively collapsed (Fig. 16).

The particular appearance of such a specimen may be explained as follows :—

The activity of the drainage mechanism is clearly sussceptible of variation. That at times it is more vigorously invoked is shown by the great distension of the periarterial lymphatics generally in cases where

œdema is marked. There are two points in connection with altered activity of the drainage that must be considered. On the one hand there may be variations in the working of the lymphatics of origin, under some conditions lymph may more readily pass into the lymph channels from the localities drained by such vessels. On the other hand, lymph may be more readily evacuated from the lymph vessels. The influence of the respiratory pump will be exerted upon the lymph vessels in the same way as it is upon the intra-thoracic veins. Augmented respiration should tend therefore to empty the lymph vessels of the lungs.

Defective drainage may be really a defect in either of these factors. As far as effective influence upon the alveolar accumulation is concerned the mere evacuation of the main lymphatic vessels may not be of great value. One could readily understand that with augmented respiration and augmented pulmonary blood flow there might be found very marked œdema and practically empty lymph channels. We imagine that the rapid respiration that occurs (frequently in the rabbit it is from 160 to 200 per minute), has assisted in the evacuation of the lymph channels, but there has been no commensurate facilitation of the passage of liquid from the alveoli into the originating lymphatics. The production of lymph has been so great that considerable alveolar accumulation has necessarily occurred. In default of other relief this has been driven into the bronchial tubes, assisted further by the movements of the lungs.

As a companion picture to the case just quoted (as an example of a type), we present the case of Rabbit XLVIII. This animal was also subjected to a sub-lethal dose of high concentration and died at about 36 hours after the experiment. It was ill after the gassing, but next morning was found alive. It had eaten a considerable amount of green food, its respiration was about 124 per minute. It seemed to get worse during the day. It was found dead and in rigor mortis the following morning. It had escaped from the run, which involved considerable exertion, and was found some distance away.

The difference between this animal and Rabbit VIII is that it was exposed to no formal exercise, but had undergone the exertion of forcing its way out of its run in the laboratory and had wandered some distance away. How long this occurred before death we have no means of judging.

Its lungs showed intense hyperæmia and œdema and examined microscopically exhibited the appearance seen in an intense case of lethal poisoning, with death at 24 hours. But here in spite of the exercise the periarterial lymphatics are greatly distended. We are disposed to think that the iuterval between the exertion and death was sufficiently long to permit the refilling of the lymphatics from the seats of origin, assuming that the exertion was sufficiently intense to account for their evacuation at any earlier epoch.

Condition of the Lung 2 Days after Gassing.—We have only a limited opportunity of examining the appearance of the lung at this stage as what we regard as a minimal lethal dose kills almost invariably within about 24 hours.

We have therefore had to depend for examination of the condition

developed in two days upon animals which have been gassed with sub-lethal doses, though occasionally we have had the opportunity of obtaining an animal which survived two days after an ordinarily lethal dose. Still, such cases must be regarded as showing relative insusceptibility, and it is perhaps not justifiable to regard them as exhibiting progressive changes in sequence with those typical at 24 hours after a lethal dose.

We take first of all the appearance exhibited by such a case (Rabbit XLIV). In many parts the lung shows but little œdema (Fig. 19). The inter-alveolar septa are perhaps somewhat thickened. In many places the alveoli, where comparatively air-filled, show fairly thick menisci of œdema fluid. In some areas considerable alveolar œdema is seen (Fig. 20), especially in sections taken from the apical regions. The bronchial tubes do not show the internal proliferation of cells seen in ordinary cases dying in 24 hours, but fairly numerous mitoses are observable in the mucous membrane, and this leads to the appearance in the channel of rather large cells resembling the alveolar macrophages we have already referred to. Since these cells are found engaged in phagocytosis we distinguish them as bronchial macrophages.* A small layer of œdema liquid is frequently seen lying against the mucous membrane, but on the whole in the less œdematous parts the channel is clear of either liquid or massed cells. In the more œdematous region the bronchial tubes contain a considerable amount of œdema liquid in which are seen polymorphs and macrophages. The free macrophages are sometimes seen exhibiting mitosis.

Those alveoli which contain much œdema liquid are somewhat contracted, looking as through the pressure of intense distension had passed off. The œdema is apparently largely replaced at the edge of the mass by epithelial cells, and a considerable number of polymorphs also invade it. In general, the œdema has a more vacuolated appearance, and in many of the vacuoles macrophages or epithelial cells are present. Extra-vascular erythrocytes are occasionally found in the œdema liquid in addition to polymorphs. These latter do not exhibit so generally the character of degeneration. The nucleus is usually compact and stains deeply. Eosinophils, which are easily distinguishable, are rather more numerous than in earlier cases. The macrophages, unless of large size, have their cytoplasm clear of pigment granules. Mitoses are not infrequent even when the macrophages are of full dimensions and disconnected from the alveolar walls (Fig. 25).

We regard this specimen as exhibiting a greater development of macrophages which apparently may go on dividing after separating from the alveolar wall. The polymorphs, though still plentiful are apparently less numerous than in cases which die at 24 hours. The eosinophils are more abundant than in the earlier stages. The œdema shows signs of having become diminished. The periarterial lymphatics are still distended (Fig. 20), indicating that it is draining away by the

* The intense proliferation of the mucous membrane seen in cases dying within 24 hours appears to have been followed by a shedding of the surface layers. There remains only a band one or two cells deep. These cells divide and some pass off at the surface, others restore the normal thickness of the mucous membrane and reconstitute the layer of ciliated cells.

normal channels, but it appears to exhibit signs which suggest a contraction of its mass, and it finds its way with other alveolar contents into the bronchial tubes. Further, it appears to suffer replacement in the alveoli by cells derived from the epithelial lining, the air-sacs showing changes characteristic of broncho-pneumonia. There is no evidence, however, of bacterial infection.

In Rabbit XLII, killed two days after a sub-lethal dose, we have a type of case which was not so severely gassed and one in which the pulmonary changes were probably at no time maximal (cp. similar case at 24 hours, page 12). By the end of two days the alveolar œdema is frequently absent in the main lobes, and the periarterial lymphatics are collapsed. Only occasionally do the bronchi show any liquid though a little cellular material may be found at places.

The interalveolar septa are thickened, though the lung was fixed in the expanded condition as shown by the circular outline of the bronchial tubes. Macrophages are rare. The most striking feature is the prevalence of eosinophils (Figs. 21 and 24). Polymorphs are still found, but they are sparse compared with the eosinophils which are prevalent everywhere, being particularly numerous in the adventitia around the arteries. Here they frequently form large masses, and they are observable also in the intima, spreading out into comparatively flat cells, and lying just within the endothelium. In the largest arteries they may be seen pervading the muscular coat (Fig. 24). Their relation to the tissues of the arterial walls will be discussed elsewhere. They may also be found in the fibrous coat of the bronchial tubes and even lying external to the epithelial layer, but they do not invade the mucous membrane to any extent. They are usually irregular in shape but compact; in some cases, however, they may be expanded and the granules scattered.

Rabbit XLIII (Fig. 22) shows that some œdema may still be found, generally in meniscus form against the walls. The periarterial lymphatics are slightly distended at places. The bronchial tubes usually contain a layer of cellular material against the walls, but are never blocked. Polymorphs are very numerous, and are presented in both expanded and compact forms. Macrophages are not very numerous, still many are seen, especially in the young stage. Eosinophils are present in increasing number over the 24 hours condition, otherwise such a case presents marked similarities to many 24 hours' cases.

We appear in these two cases to have exhibited two stages in the course of the changes, XLIII being less advanced than XLII, though both were killed after the same interval. The evidence suggests that with the disappearance of the œdema the polymorphs become fewer and eosinophils increase in number.

Macrophages seem to vary as regards their number in different animals and at different stages. Where there is much cellular material in the bronchial tubes, many macrophages are included; these may come either from the alveoli or more directly from the mucous membrane of the tubes. These cells are frequently quite numerous in lethal cases after 24 hours; they attain prominence earlier than the eosinophils. But we have only seen them really numerous at three days after gassing (see next section.)

Condition of the Lung three days after Gassing with a Sub-lethal Dose.—No sharp line can be drawn between the respective appearances in passing from two days to three days. In many cases examples of the lung at three days are indistinguishable from earlier stages; there may be even less progress towards repair than in a two-day case. If the natural reaction of the lung to the stimulus of the poisonous gas is not immediate and well developed (and the evidence of this, as far as one can tell, is the very early polymorpholeucocytosis), then presumably the resultant changes are protracted and the disappearance of the œdema in a non-fatal uncomplicated case may frequently take several days at least. Thus, in the third day, one meets cases in which the œdema still persists in some areas, though it shows obvious signs of diminishing. These signs are the lessening of the pressure apparently exerted in the neighbouring structures. The alveolus is no longer approximately circular in optical section, or compressed by adjacent pressure into some departure from the circular, but yet of a shape which indicates internal distension. It is now somewhat shrunken and the œdema liquid may be reduced so that in addition to the usual peripheral vacuolation, it is largely honeycombed with spaces (Fig. 27), which may or may not contain cells of different kinds. The last relics of œdema frequently are seen to consist of a few bands of homogeneous substance of varying width. Sometimes a condition approaching collapse may be seen, a small relic of œdema centrally and approximately cubical cells, and polymorphs at the periphery. At times the whole alveolus, somewhat shrunken, is filled up with a mass of epithelial cells and a few polymorphs. The defining of the territory of an alveolus is frequently a difficulty in the standard-stained specimens; we therefore have relied for this purpose largely on specimens stained by Weigert's process for demonstrating elastic tissue.

These cases which represent protracted pulmonary change not infrequently give us the opportunity of observing in more detail the stages of certain developments.

In the first place the appearances in the second stage of the changes in the bronchi are made clearer.* The first stage we regard as represented by the proliferation and apparent segmentation of cells of the mucous membrane, the results of which are largely thrown off into the cavity, leaving little more, in severe examples, than the basal cells. These basal intercalated cells in the second stage of repair show mitoses (Cp. Fig. 23). The results of the division originate new columnar cells in part and other cells which do not align themselves in the phalanx of the columnar epithelium, but which ascend towards the surface and undergo frequently further mitotic division in the ascent. These are finally set free on the surface. Many polymorphs and occasionally eosinophils also invade the epithelium and pass to the surface. The polymorphs are somewhat swollen, and show in their transit a very irregular outline, the granules are dispersed. In our interpretation of the appearances we should regard them as active polymorphs. When they have reached the cavity of the tube they assume a more spherical shape, tend to fuse with one another, the nuclei stain more intensely

* See Fig. 23, showing 2-day changes. Rabbit XLIV.

and become fragmentary, the granules are still recognisable though less clear.

It is noteworthy that more delay towards reparative processes is shown (in the rabbit) in the apical portion of the lung than in the basal regions. Frequently a section through the apex will exhibit changes characteristic of 24 hours, whilst considerable advance in resolution of the œdema is observable at the base.

The lungs of Rabbit XLVI, exhibit changes similar to those described above. Many examples of the activity of the macrophages are seen, though in these two lungs they are not excessively numerous. All stages from the condition of a cubical epithelial cell to the fully formed and swollen macrophage can be found. There are sometimes to be seen masses, plum-coloured with the standard stain, consisting of apparently closely packed masses of degenerate erythrocytes. These are occasionally found in contact with a macrophage, and almost identical bodies may be seen actually within the macrophage. We consider these are degraded erythrocytes which become ingested and finally account for some of the brown pigment granules seen in the macrophages.

Rabbit III had been exposed to about one half of a lethal dose, but at the end of the second day had been placed under luminal and was kept under the drug till it died at the end of the third day. The lung of this animal showed a very marked development of macrophages, and the phagocytic processes could be well studied in their different stages.

In many alveoli there is no œdema whatever visible, if at any time there had been it had become cleared up. In such clear alveoli in many cases large numbers of free macrophages are visible (Fig. 26). These appear generally in the fully expanded or swollen condition, but some are visible of a smaller size, and, further, still smaller ones may be observed attached to the alveolar walls. In the more collapsed part, the thicker epithelium and attached macrophages present intermediate stages. There seems every reason to regard these macrophages as originally epithelial cells of the alveolus. We have not been able to satisfy ourselves of any evidence showing that they originate from the blood in the same way as the polymorpho-nuclear cells. While still attached to the alveolar walls, though bulging into the air space they may exhibit foreign inclusions, *e.g.*, erythrocytes and polymorpho-nuclear cells, and by digestion of these they presumably become endowed ultimately with dark pigment granules not unlike carbon particles, shown quite plentifully in the young free condition (Fig. 26A). These macrophages may be found, in such a specimen as the lung of Rabbit III, in large numbers in the bronchial tubes and here they may be added to, to some extent, by cells budding off from the epithelium of the mucous membrane. In such alveoli as show œdema macrophages may also be found. The polymorphs occur in diminishing number, the eosinophils are more prominent. We interpret this specimen as showing the appearance characteristic of second or third day in an animal which was not heavily gassed, in which the œdema was probably never maximal, and in which the repair processes had advanced. The presence of the macrophages suggests a scavenging

process in full vigour, a removal of polymorphs and erythrocytes from the alveolus, the œdema being drained off largely by the lymphatics. The macrophages and cell relics pass off mainly by the bronchial tubes.

Condition of Lung 4 days after Gassing with a Sub-lethal Dose.—This may be regarded as exhibiting early stages of recovery processes, much less advanced in the apex than in the lower lobes as is commonly the case. In the apical region there is still a considerable amount of alveolar œdema, particularly near the surface. The periarterial lymphatics are not distended. These show signs of dilation but contain no fluid. This suggests that probably the œdema fluid in the alveoli may have undergone solidification. It shows the vacuolation characteristic of the recovery process, but there is no appearance of fibrin formation. In some alveoli in which only a few relics of œdema are found macrophages are conspicuous and their activity may account for the disappearance of the œdema. Where only a relic of œdema can be seen this is frequently represented by a non-homogeneous granular substance incompletely filling the space which now largely contains air and a variable number of macrophages. Eosinophil cells are very conspicuous both in alveolar walls and in the adventitia of the arteries. In this latter situation, particularly with the smaller arteries, they may form a kind of ring several cells deep somewhat closely massed together (Fig. 28). Polymorphs are not numerous.

The epithelium of the bronchi is approximately normal with but little invasion by polymorphs. The bronchi contain material which consists of macrophages, polymorphs with fragmentary nuclei, a few eosinophils, some plum-coloured masses, all lying in a matrix of what appears to be mucous substance, but which is partly escaped œdematous material.

In the basal region the œdema has almost vanished. The bronchial tubes are practically normal. The alveolar septa are thickened. They contain many large nuclei some of which are presumably concerned with macrophage production. At places, especially where there is collapse, the lining membrane is of a low cubical variety in some portions of the alveolar walls. Polymorphs are not numerous. Eosinophils are present in fairly large numbers. In a few places a small amount of homogeneous œdema is still visible and the partly collapsed alveolus contains may epithelial cells filling up the air-space around the patch of œdema. Generally where any remains of œdema can be recognised these are represented by strands of granular material loose in texture and stretching incompletely across the alveolus. For the greater part the alveoli are distended simply with air, but the walls are distinctly thickened.

The apical part is less advanced in progressive change than the basal, where the appearances are more indicative of repair. The characteristic signs of this appear to be the diminishing œdema, the increase in epithelial cell production, the well marked local eosinophilia, and the less conspicuous presence of polymorphs. The epithelial cells may have two destinies, either to re-establish the lining of the wall or to bud off and assist in clearing away the dead alveolar material, including erythrocytes, solidified œdema or polymorphs.

Condition of Lung after marked Destruction of Tissue.—The degree

of destruction of tissue, in terms of depth rather than surface, present in the earlier stages is not easy to estimate. An animal dying within 24 hours after a lethal dose may have considerable damage done to the alveolar wall though this damage is not histologically manifest in so short a period. With sub-lethal doses it does not usually appear that there is any appreciable damage to the essential structures of the wall. The surface layers of the mucous membrane of the bronchi may be destroyed and cast off, and to some extent this is the case with the alveoli. But on the reasonable assumption that the macrophages are active living cells budded off from the pulmonary epithelium (presumably from the more cubical granular cells that lie in the meshes of the capillary network), this epithelium seems to be, in such cases, possessed of considerable resistance. The squamous cells covering the capillaries are not infrequently destroyed.

Apparently at times the extent of the destruction is great, and the whole substance of the alveolar wall including even the elastic tissue is affected. We are satisfied that this is not a change secondary to micro-organic infection. Provided the area of the lung thus intensely affected is not too great, the animal may live. We have in Rabbit X such a case, where the animal was killed on the seventh day after gassing.

Here the lung has practically lost its alveolar structure, though elastic tissue preparations will still indicate the original boundaries of the air cells. But the elastic tissue is greatly diminished in quantity as can be readily shown by comparing these consolidated areas with adjacent areas less affected (see Figs. 29 and 30). The whole alveolar cavity is filled up with a mass of polymorphs with a few eosinophils and some epithelial cell relics. The blood vessels seem to be usually choked with a cell infiltration which is probably proliferated from the endothelium. The appearance of such an area is that of a massive accumulation of polymorphs extending in circular bays into the less deeply affected region adjacent. Small islands of such tissue may occasionally be seen (Fig. 31). There is a marked resemblance to a number of isolated or confluent focal abscesses, though no obvious breaking down of the material occurs. Some œdema may be present.

We have not had the opportunity of tracing the further changes that such tissue undergoes.

SUMMARY.

1. There seems to be reason to believe that there normally exists in the lung a comparatively vigorous lymph production and drainage by lymphatics. Increase of pulmonary blood pressure would rapidly augment this production. The respiratory movements probably actively assist in evacuating the perivascular lymph vessels. The drainage in the rabbit's lung is mainly by the periarterial lymphatics.

2. As the result of gassing with a lethal dose alveolar œdema is not obviously apparent in the rabbit till after the first hour. The periarterial lymphatics show some distension before there is any evidence of alveolar œdema (augmented drainage balancing augmented production). In an animal dying in about 24 hours after a lethal

dose there is much alveolar œdema, and the periarterial lymphatics are greatly distended (drainage unable to compensate augmented production). The œdema in some cases becomes fibrinous.

3. Rabbits may die as the result of forcible exercise after a considerable but still sub-lethal dose. In such animals there is intense alveolar œdema, but the periarterial lymphatics are collapsed. This is probably to be explained as the consequence of evacuation of lymphatic vessels by the greatly increased respiratory movements. In rabbits gassed with strong sub-lethal doses the œdema shows signs of becoming reduced at about the second day. Alveolar œdema may be found in varying amounts as late as the seventh day.

4. Within the first two hours a considerable invasion of polymorphonuclear leucocytes is apparent. In animals dying in 24 hours after a lethal dose very large numbers of polymorphonuclear leucocytes are usually found. In some cases animals gassed with what are normally sub-lethal doses die within two days, and in such cases the local polymorphonuclear leucocytosis is poorly shown. We regard the invasion of polymorphonuclear leucocytes as probably evidence of a beneficial reaction.

5. Rather later than the invasion of polymorphonuclear leucocytes numbers of large mononuclear cells appear which we regard as of epithelial origin. They frequently show mitosis, and are actively phagocytic even while still adherent to the alveolar wall. They appear to possess a scavenging function.

6. At a still later date (about the third day) a marked invasion of eosinophils is apparent. The eosinophils are particularly conspicuous in the adventitia of the arteries. Simultaneously the polymorphonuclear leucocytosis seems to diminish.

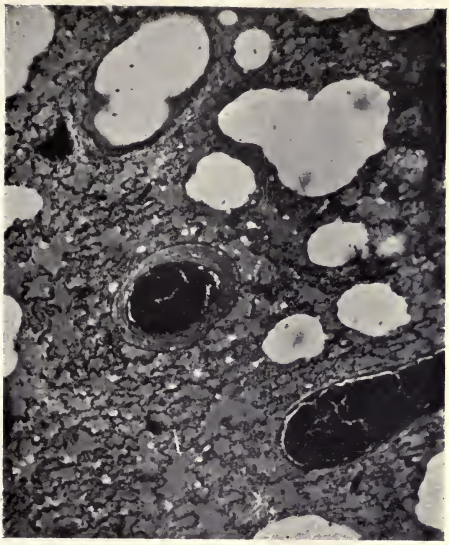

FIG. 1.—Lung of rabbit XLVIII. Marked œdema. Arteries, veins, and capillaries much distended with blood. Lymphatics around arteries maximally distended, peribronchial and perivenous not evident.

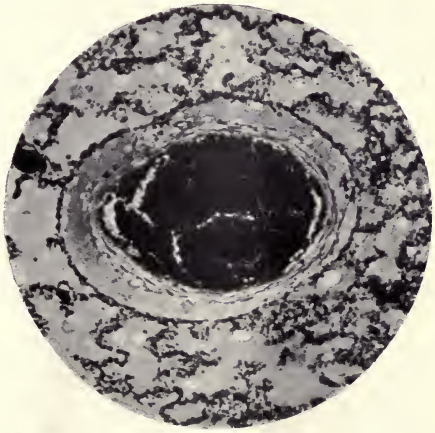

FIG. 2.—Artery of Fig. 1 more highly magnified. Distended periarterial lymphatics forming a ring about twice the width of the stretched muscular coat.

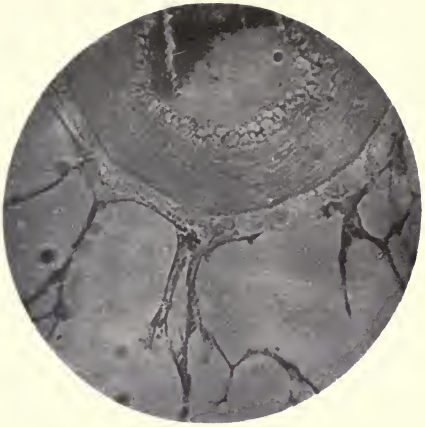

Fig. 3.—Lung of rabbit XXXVIII (high power magnification). Slight distension of periarterial lymphatics. Afferent alveolar lymphatics opening into periarterial contain lymph and small mononuclear leucocytes. (Pappenheim's stain.)

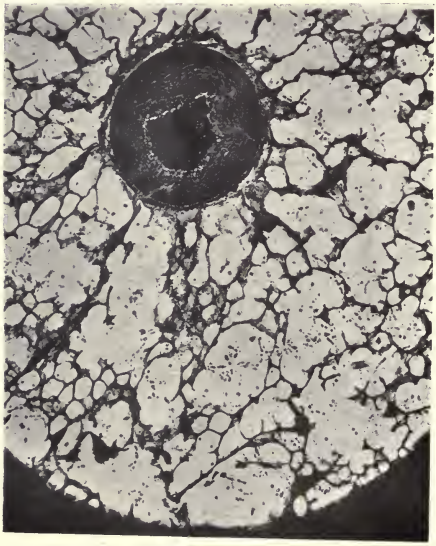

Fig. 4.—Lung of rabbit XXXVIII (low power). No obvious alveolar œdema.

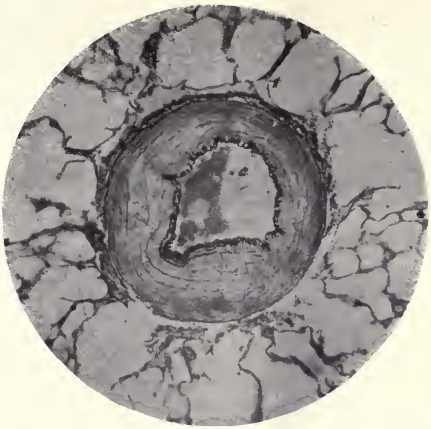

FIG. 5.—Lung of rabbit XXXVIII. Commencement of distension of periarterial lymphatics. (Weigert's elastic stain.)

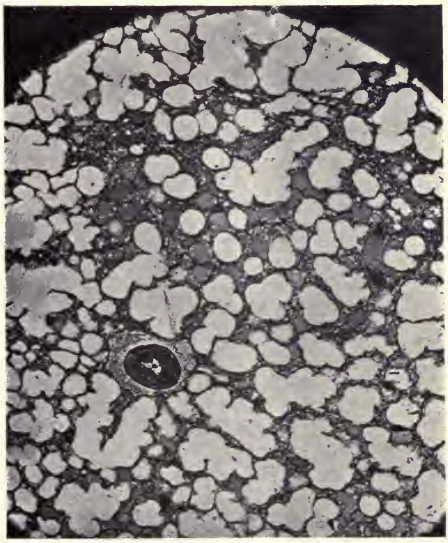

FIG. 6.—Lung of rabbit XXXIX (two hours after gassing with minimal lethal dose). Progressing alveolar œdema and well-marked distension of periarterial lymphatics.

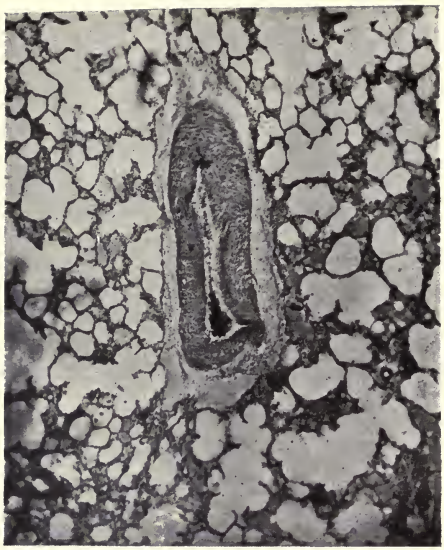

FIG. 7.—Lung of rabbit XXXIX (two hours after gassing with minimal lethal dose). Progressing alveolar œdema and well-marked distension of periarterial lymphatics.

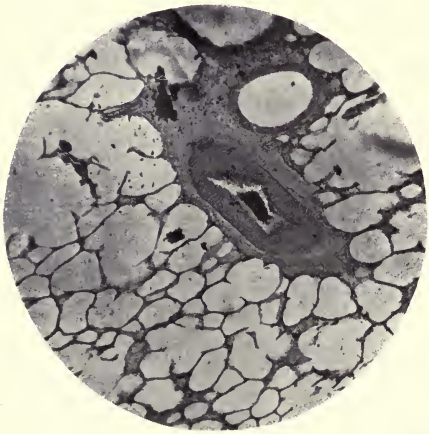

FIG. 8.—Lung of rabbit XLI ($5\frac{1}{2}$ hours after gassing with a sub-lethal dose of high concentration). Very little œdema. Periarterial lymphatics well distended.

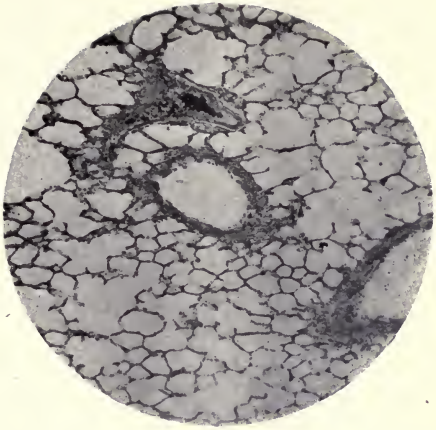

FIG. 9.—Lung of rabbit XL (24 hours after gassing with a sub-lethal dose of high concentration). Practically no alveolar œdema.

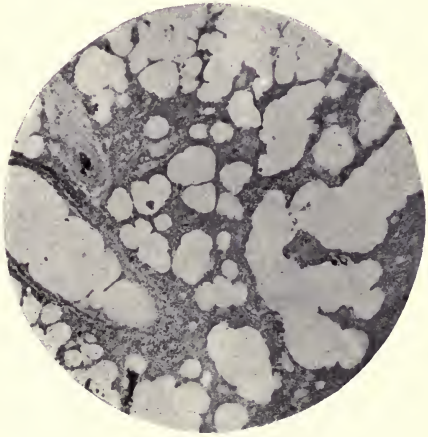

FIG. 10.—Lung of rabbit XL (24 hours after gassing with a sub-lethal dose of high concentration). Fair amount of alveolar œdema.

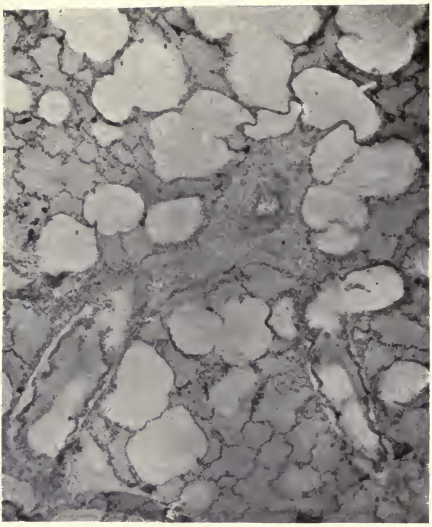

FIG. 11.—Lung of rabbit XVI. (Animal died 24 hours after gassing with a lethal dose.) General œdema. Distended periarterial lymphatics. Proliferation of bronchial mucosa. Œdema in bronchi.

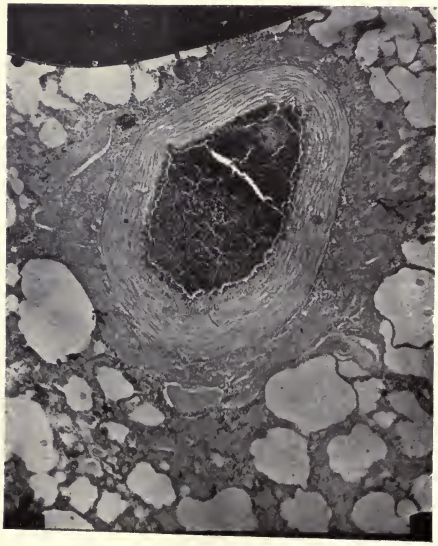

FIG. 12.—Lung of rabbit XIX. Distended periarterial lymphatics.

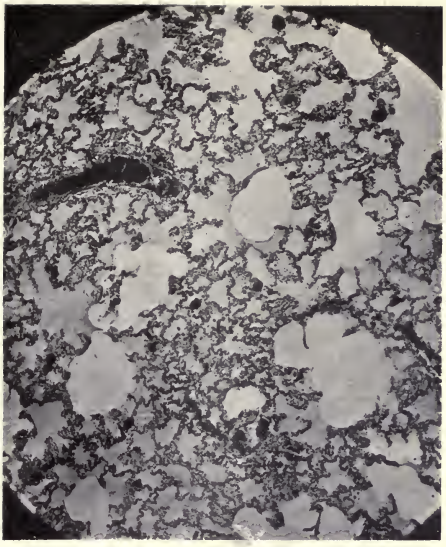

FIG. 13.—Lung of cat. (Animal died five hours after gassing with a lethal dose.)

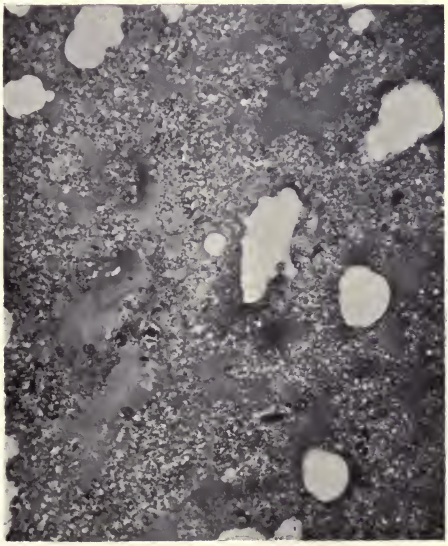

FIG. 14.—Lung of rabbit XXIII. (Animal died 24 hours after gassing with a lethal dose.) Unequal development of œdema. Collapsed alveoli and islands of œdema.

FIG. 15.—Lung of rabbit VIII. (Animal died 24 hours after gassing with a sub-lethal dose, as the result of exercise.) A little periarterial distension.

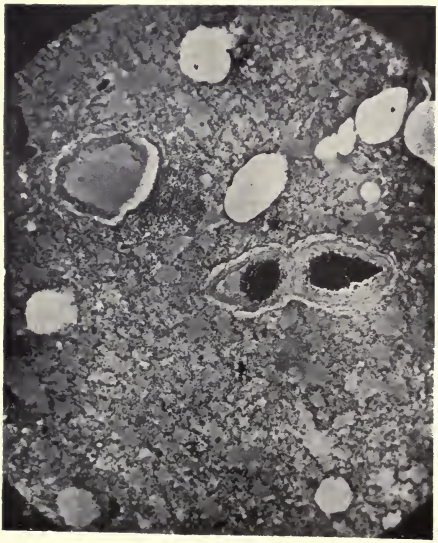

FIG. 16.—Lung of rabbit VIII. (Animal died 24 hours after gassing with a sub-lethal dose as the result of exercise.) Collapsed lymphatics. Bronchi full of œdema.

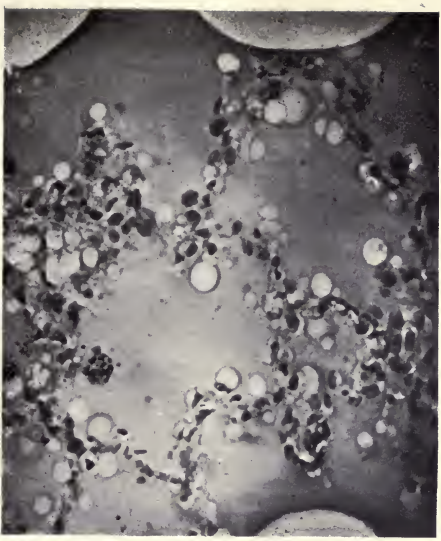

Fig. 17.—Lung of rabbit VIII. (Higher magnification.) Œdematous alveoli, macrophages in phagocytosis, peripheral vacuolation.

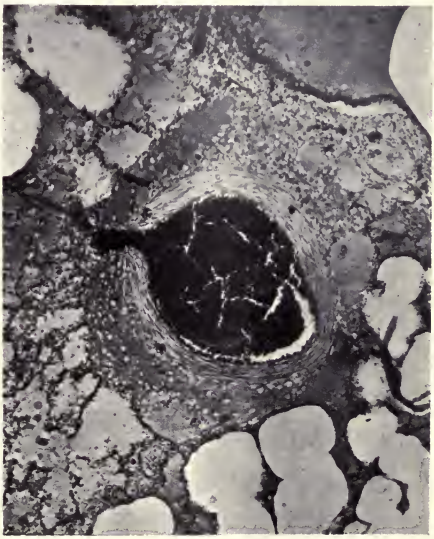

Fig. 18.—Lung of rabbit XLVIII. (Animal died about 40 hours after gassing as the result of exertion. No formal exercise.) Periarterial lymphatics distended.

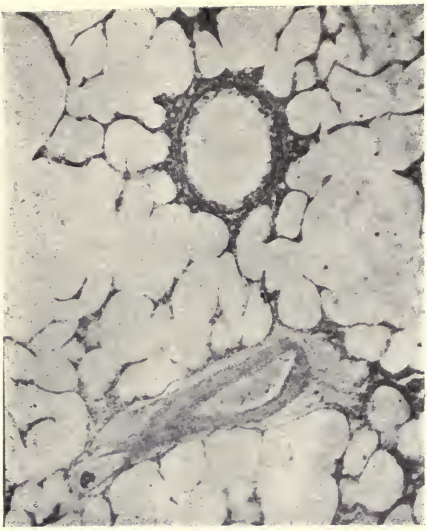

FIG. 19.—Lung of rabbit XLIV. (Animal killed two days after gassing with a sub-lethal dose of high concentration.) Little œdema.

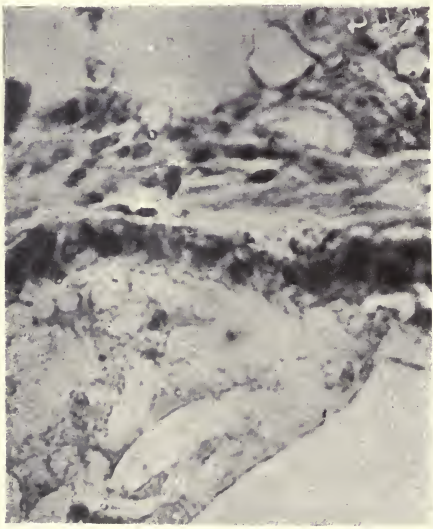

FIG. 20.—Lung of rabbit XLIV. (Animal killed two days after gassing with a sub-lethal dose of high concentration.) A more œdematous part. Repair of bronchial mucous membrane.

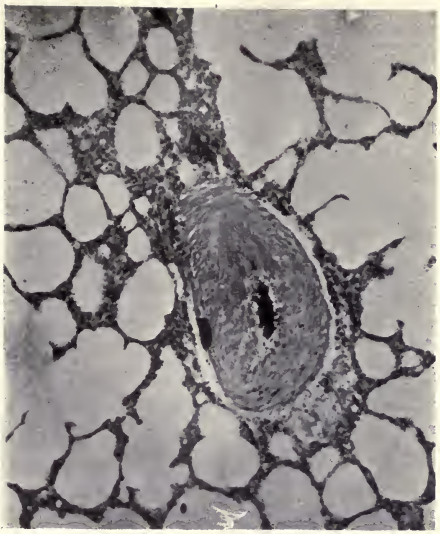

FIG. 21.—Lung of rabbit XLII. (Animal killed two days after gassing with a sub-lethal dose of high concentration.) Practically no œdema. Thickened septa. Many eosinophils in arterial coats.

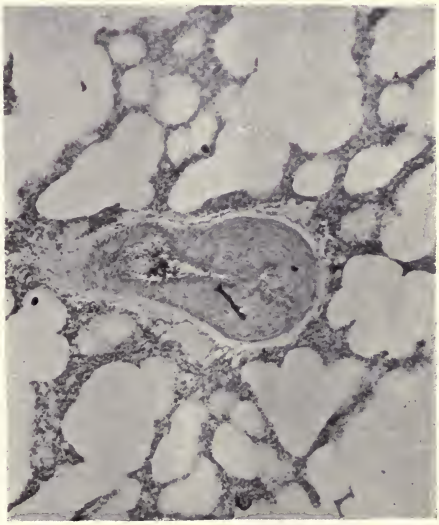

FIG. 22.—Lung of rabbit XLIII. (Animal killed two days after gassing with a strong sub-lethal dose.) Some œdema. Thickened septa.

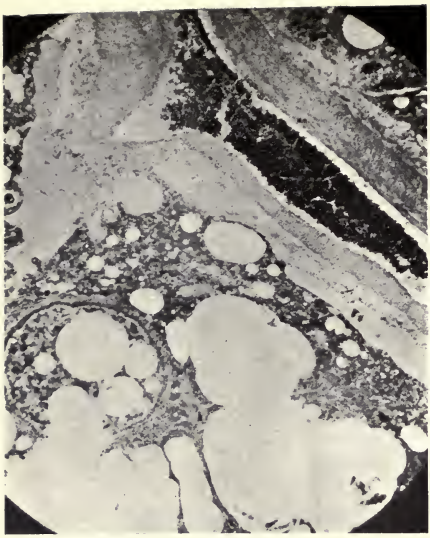

FIG. 23.—Lung of rabbit XLIV. (Animal killed two days after gassing with a strong sub-lethal dose.) Process of repair of bronchial mucous membrane reduced to one cell thickness. Two mitoses are visible.

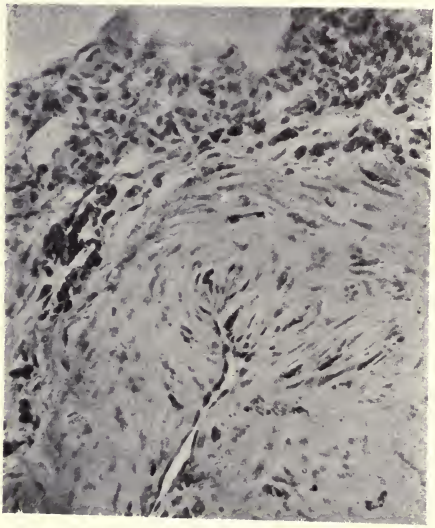

FIG. 24.—Lung of rabbit XLII. (Animal killed two days after gassing with a strong sub-lethal dose.) Epithelial invasion of arteries. The dark cells are the eosinophils, and are seen abundantly in the adventitia and in the mucous coat of the artery.

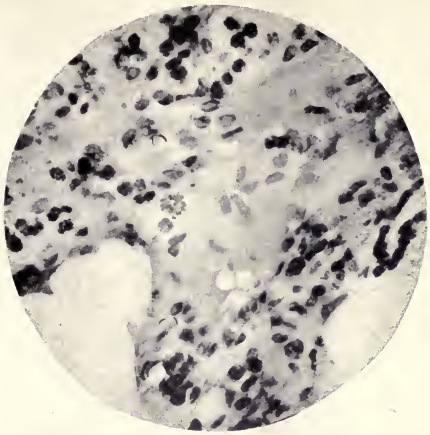

FIG. 25.—Lung of rabbit XLIV. (Animal killed two days after gassing with a strong sub-lethal dose.) Mitosis in macrophage of full size.

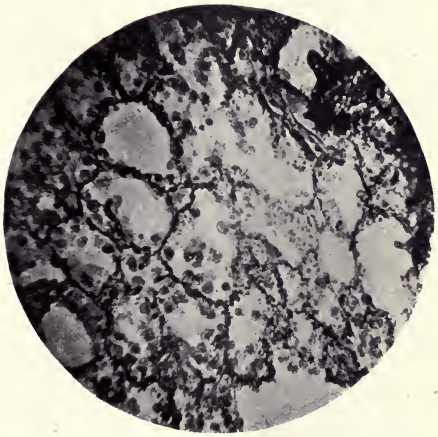

FIG. 26.—Lung of rabbit III. (Animal died three days after gassing.) Maximal production of macrophages.

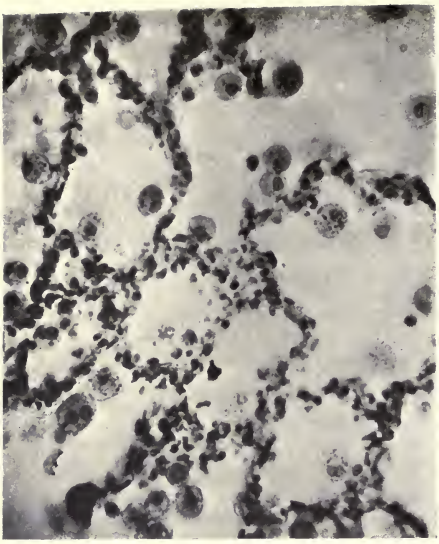

FIG. 26A.—Lung of rabbit III. Part of Fig. 26 more highly magnified. Showing the cell inclusions in the macrophages in addition to the carbon particles, &c.

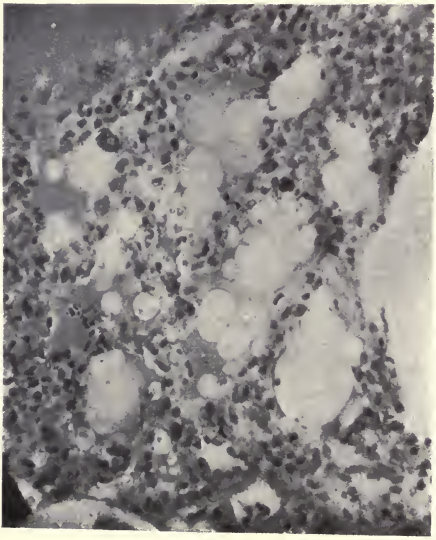

FIG. 27.—Lung of rabbit XLVI. (Animal killed three days after gassing with a strong sub-lethal dose.) Vacuolation of œdema seen in process of reduction.

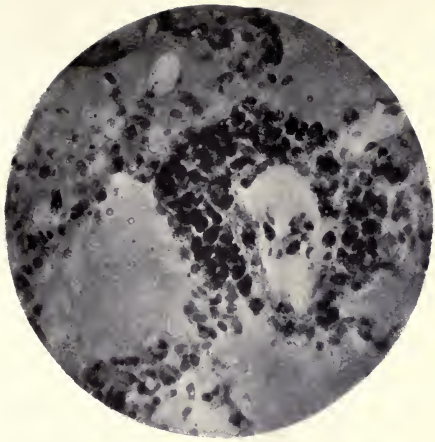

FIG. 28.—Lung of rabbit XLIX. (Animal killed four days after gassing with a sub-lethal dose of high concentration.) Ring of eosinophil cells around small artery.

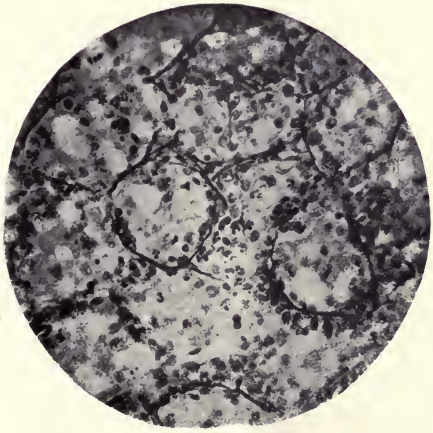

FIG. 29.—Lung of rabbit X. (Animal killed seven days after gassing with a strong sub-lethal dose.) A less affected part showing considerable elastic tissue. (Weigert's elastic stain.)

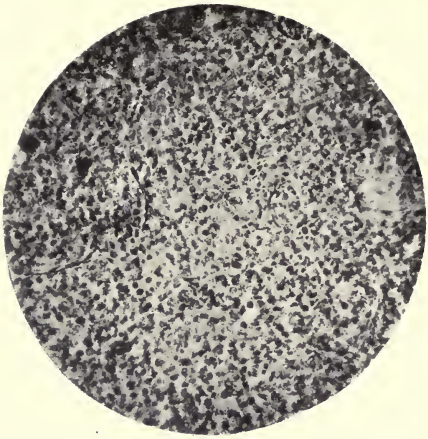

FIG. 30.—Lung of rabbit X. (Animal killed seven days after gassing with a strong sub-lethal dose.) A portion of lung crowded with polymorphs. Only occasional strands of elastic tissue are visible. (Weigert's elastic stain.)

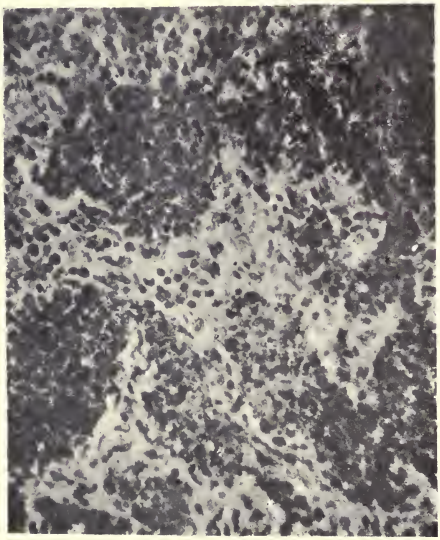

FIG. 31.—Lung of rabbit X. The darker areas represent accumulations of polymorphonuclear leucocytes. (Compare with Fig. 30, which shows the relics of alveolar territories.)

II.—A REPORT ON THE MICROSCOPIC LESIONS CAUSED BY THE INHALATION OF DICHLORETHYL SULPHIDE VAPOUR IN THE CAT.

By H. M. Carleton.

(*From the Physiological Laboratory of Oxford University.*)

The material upon which the following observations are based was fixed immediately after death in corrosive-acetic or picro-formol-acetic. The sections were stained in Friedländer's hæmatoxylin or iron hæmatoxylin followed by eosin or orange-G. Both cats were killed with chloroform.

Cat No. 1.

Exposed to dichlorethyl sulphide for 2 *hours*, killed four days afterwards.

Trachea (upper part).

(*a*) *Fibrous Tissue.*—Many lymphocytes at large. Normal in other respects.

(*b*) *Submucous Areolar Tissue.*—Intense leucocytic infiltration is observable, especially in the posterior region between the two horns of the cartilage rings. The blood vessels are very distended and contain many polymorphs. Many of the mucous glands and ducts are necrotic, staining diffusely.

(*c*) *Mucous Layer.*—The ciliated epithelium has disappeared except over small areas where it is still visible, though clearly necrotic.

In the lumen there is a ring-like cast of clotted blood packed with lymphocytes and polymorphs. The centre of the trachea is free.

Trachea (lower region, just above the bifurcation).—Here necrosis is still more marked than in the upper portion.

(*a*) *Fibrous Layer.*—Intense leucocytic invasion is observable throughout this region.

(*b*) *Sub-mucous Layer.*—Here necrosis is very advanced. In those parts the least affected, the mucous glands of the areolar tissue are still discernible. The leucocytic invasion is intense; there are numerous polymorphs in the ducts of the mucous glands and in the areolar tissue which is clearly undergoing disintegration. The blood vessels are greatly dilated and in many places disorganised so as to form areas of hæmorrhage.

(*c*) *Mucous Layer.*—This is altogether absent over large areas. In some places, *e.g.*, at the point where the duct of a mucous gland opens on to the surface of the trachea, the epithelial layer is still visible as a sheet of œdematous, diffusely staining and obviously dead cells. The lumen is entirely filled by a vacuolated plug composed of polymorphs, lymphocytes and disintegrating red blood corpuscles, the latter are central, the two former most abundant peripherally.

The Lungs and Bronchi.

(*a*) *The Main Bronchi.*—The general condition is the same as in the lower part of the trachea, *i.e.*, leucocytic infiltration and desquamation of the bronchial epithelium over the greater area of the bronchus. In some places the epithelium is undergoing separation from the underlying tissue by pressure of extravasated blood. The lumen is occupied by a ring-like mass of lymphocytes and polymorphs. There is no blood clot while the centre of the lumen is free.

(*b*) *The Smaller Bronchi.*—The general inflammatory condition is as in (*a*), but more intense in most of the bronchi examined. Some of the bronchi are almost completely disintegrated, lying in a mass of leucocytes. The lumen is generally completely occluded by a vacuolated plug of lymphocytes and polymorphs.

(*c*) *The Alveoli.*—Here as elsewhere the chief feature is acute leucocytic infiltration and general disintegration varying in degree. In large areas the alveoli are blocked internally and surrounded by masses of leucocytes. Over some areas there is much extravasated blood. In other regions the alveoli are remarkable in that they each contain a mulberry-like mass of large cells. In what seem to be the earlier stages of this condition the mass is adherent to the alveolar wall, while later it lies freely within the alveolus.

From the material I have examined I am led to think that these cell-conglomerations in all probability represent the alveolar epithelium in an extraordinarily œdematous condition shed into the alveolar cavity. Within some of these cell-masses the original alveolar cavity, now greatly reduced, is still apparent. These masses are not to be found usually in the bronchi.

In many areas of the lung abcesses have formed, leading to the destruction of all the tissues with the exception of some of the cell-masses described above.

Cat No. 2.

Exposed to the effect of dichlorethyl sulphide for 1¼ *hours*, killed nine days afterwards with chloroform, when the animal was obviously on the way to recovery.

Trachea.—A portion from the middle of this was sectioned and examined.

(*a*) *Fibrous Layer.*—Normal.

(*b*) *Submucous Layer.*—Polymorphs are present in large numbers in the blood vessels of the areolar tissue. The mucous glands are normal.

(*c*) *Mucous Layer.*—The epithelium is complete in most places. Here and there, however, it has disappeared, leaving the lymphoid tissue exposed. While the epithelium is quite normal over many regions it is invaded with polymorphs in others, and in those areas where inflammation is the most intense it is œdematous and undergoing disintegration. The lumen is clear except for occasional epithelial cells around its periphery.

The Main Bronchi.—In these the epithelium is intact though covered with a thin layer of mucous. On one side there is a thicker mass of clotted blood containing cell-débris. Apart from these formations the tissues seem normal.

The Smaller Bronchi.—The epithelium is intact in many places; in others it shows signs of disintegration. In some bronchi desquamated epithelial cells containing pigment particles are visible in the lumen. No leucocytic infiltration is observable.

The Alveoli.—The alveolar walls are thickened and in many places invaded by polymorphs. The alveolar cavities are somewhat collapsed and do not contain leucocytes.

The Blood Vessels are abnormally dilated.

Of the other organs the following were examined :—

The Liver.—Many of the lobules present a vacuolated appearance suggestive of some form of fatty degeneration. It is impossible to say whether this condition is due to the effect of the gas or not.

The Kidneys are apparently perfectly normal histologically.

The Stomach, normal.

The Skin of the Ears reveals invasion of the epidermis by polymorphs. There is no desquamation. The blood vessels contain a rather large number of leucocytes. No pigmentation is observable.

The Nasal Epithelium.—Here there is evidence of desquamation in places where there is intense leucocytic infiltration.*

Summary.—The histological lesions are far more marked in Cat No. 1 than in Cat No. 2. This is as one would expect in view of the fact that the former was exposed to the action of the gas for a longer period (2 hours), and killed after a shorter time had elapsed (4 days). than was the case with the latter which was gassed for 1¼ hours and killed 9 days afterwards. The chief microscopic changes found in

Cat No. 1 are :—

(1) The desquamation of the tracheal epithelium.
(2) The formation of an inflammatory plug of leucocytes and red blood corpuscles.
(3) Lesions of a similar kind, though far more severe throughout the bronchial tree.
(4) The leucocytic invasion of the alveoli together with the œdema and desquamation of the alveolar epithelium.
(5) The formation of numerous abcesses.

In *Cat No.* 2 the chief features are :—

(1) The thickening and collapse of the alveolar walls.
(2) The dilated condition of the blood vessels of the lung.
(3) The inflammatory condition of the epidermis of the ears.
(4) The desquamation of the nasal epithelium.

August 31*st*, 1917.

* Further material was examined after the above was written. I find the infiltration intense over most areas and extravasated blood was also observed

III.—REPORT ON HISTOLOGICAL EXAMINATION OF HUMAN TISSUES FROM CASES OF POISONING BY DICHLORETHYL SULPHIDE.

By J. Shaw Dunn, Capt., R.A.M.C.

(*From the Porton Laboratories.*)

(Material sent from No. 7 General Hospital by C. D. Rankin, Capt., R.A.M.C.)

Case 1.

Gassed 21/7/17. Died 25/7/17.

Bronchus.—The epithelial layer is entirely destroyed, and is replaced, for the most part, by a thick layer of fibrin with débris and leucocytes, resembling the membrane in diphtheria. The deeper layers of mucous membrane are also affected; there is thrombosis of small arterioles, and much œdema: the elastic-tissue fibres are swollen.

Lung.—The lung-tissue shows patchy consolidation, and œdema. The alveoli are filled mainly by granular residue of œdema and fibrin reticulum; leucocytic exudate is abundant in certain groups only. There is no certain evidence of destruction of alveolar walls, or of capillary thrombosis. All the smaller bronchioles are markedly damaged.

Kidney.—Congested. There is no certain alteration recognisable in the renal epithelium or glomeruli.

Suprarenal.—No changes apparent.

Liver.—No evidence of cellular degeneration or other pathological change.

Case 2.

Gassed 21/7/17. Died 31/7/17.

Lung.—There is well-marked patchy consolidation as in ordinary broncho-pneumonia: the intervening freer areas of lung show slight œdema. The solid patches centre around badly-damaged alveoli: the latter are filled by dense masses of necrotic débris carrying very large numbers of micro-organisms, chiefly cocci. There is some destruction of alveolar walls in these situations. The exudate is largely hæmorrhagic but also contains some fibrin, granular residue of œdema, leucocytes and catarrhal cells. In some areas there are large tracts of solid œdema which correspond with bronchioles choked by masses of débris.

Case 3.

Gassed 21/7/17. Died 25/7/17.

Lung.—Well-marked broncho-pneumonia with abundant hæmorrhagic and purulent exudate. There is much damage of infundibula: these are plugged by masses of necrotic débris, containing very large numbers of micro-organisms.

Case 4.

Gassed 21/7/17. Died 25/7/17.

Lung.—There is patchy broncho-pneumonia with exudate chiefly purulent. Only slight evidence of œdema in places.

Bronchi and Bronchioles exhibit the same severe penetrating lesion as in Case 1 : it closely resembles the lesion in diphtheria.

Kidney.—Apart from congestion there is no noteworthy change.

Spleen, Heart, Liver and Intestine.—No changes apparent.

Summary.

The most noteworthy features are : (1) The severe and lasting damage of the bronchi and bronchioles ; (2) the persistence of œdema ; (3) the severe degree of infection and broncho-pneumonia, with hæmorrhagic exudate in two cases.

No evidence of remote effects is found in the portions of organs, other than the lungs, examined.

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REPORTS

OF THE

CHEMICAL WARFARE MEDICAL COMMITTEE.

No. 3.—THE SYMPTOMS AND TREATMENT OF THE LATE EFFECTS OF GAS POISONING.

10*th April*, 1918.

In January, 1918, the Director-General, Army Medical Service, with the concurrence of the Controller of Chemical Warfare, appointed the following Committee to prepare reports, based upon information received from all sources at the Chemical Warfare Department, for submission to him with a view to their distribution to those concerned, to make suggestions for further co-ordinated medical investigations that they seem desirable, and to advise him generally in respect of the scientific medical aspects of Chemical Warfare :—

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Professor W. M. Bayliss, D.Sc., F.R.S.
Professor A. E. Boycott, M.D., F.R.S., Capt. R.A.M.C.
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Italy :—

Colonel S. L. Cummins, C.M.G., M.D.

Reports of the Chemical Warfare Medical Committee.

No. 1. Notes on the Pathology and Treatment of the Effects of Irritant Gases.

No. 2. The Histological Effects produced by Gas Poisoning and their Significance.

(C 1082) Wt. —117 5½M 4/18 H & S

THE SYMPTOMS AND TREATMENT OF THE LATE EFFECTS OF GAS POISONING.

The gases used most commonly by the enemy are of three main varieties :—

(1) Suffocative: for example, Chlorine, Phosgene ($COCl_2$), Diphosgene, Chloropicrin ($CCl_3 NO_2$).

(2) Vesicants: Dichlorethyl sulphide $(C_2H_4Cl)_2$ S. (Mustard Gas or Yperite).

(3) Pure Lachrymatory: for example, Xylyl-bromide.

Gas may be liberated from cylinders (cloud gas) or from shells.

Cloud Gas Attacks.

The gas is liberated from cylinders, and drifts forward on the wind. Chlorine alone was used in the first attacks of April and May, 1915. In December, 1915, Phosgene was used together with Chlorine, and this mixture was repeated in the attacks from April up to August, 1916. Since that date no cloud gas attacks have been made by the enemy against the British front.

Gas Shells.

At first these only contained lachrymators, which affected vision for a short time, but produced no other serious, and no lasting, effects. In the autumn of 1916 lethal gas shells were used; these contained Phosgene, Chloropicrin, and other allied lung irritants in varying proportions. In July the enemy introduced another shell, "Yellow Cross," containing the new substance, "Mustard Gas." Shortly after this, shells containing organic arsenic compounds such as diphenylchlorarsine, were also brought into use, the shell being marked as "Blue Cross" or "Red Cross."

The general aim of the enemy in the present use of gas shells is to fire simultaneously shells of different types, some of which will cause so much sensory irritation that the man will discard his respirator, and then become vulnerable to lethal shells containing Phosgene and similar substances. Owing to this mixture of shells the symptoms reported by patients are often very confusing.

Action of Gases.

1. *Suffocative.*—These gases act mainly on the alveolar epithelium of the lungs, causing acute œdema of the lungs, of very rapid onset, and thrombosis of the pulmonary capillaries. They have less effect on the air passages, but may have an irritant action on the pharynx, larynx, and bronchi. Chloropicrin is a powerful lachrymator, but Chlorine and Phosgene do not affect the eyes to any great extent.

Early Symptoms.—The immediate effects of irritation of the eyes may be prominent at first, but as a rule quickly pass off; within 3 to 12 hours after exposure to the gas the main symptoms, asphyxia and prostration, due to affection of the lung alveoli and accumulation of fluid in them, appear. In this stage the patient's respiration is

rapid and usually accompanied by pain (often intense) in the chest; there may be violent fits of coughing, but the amount of expectoration is very variable, being profuse in some cases, and very scanty in others; in the more severe cases the patient is restless and anxious, or may be semi-comatose with muttering delirium. Therefore many patients will be unable to give a definite account of their symptoms as loss of memory of immediate events may last for several days. Patients with severe pulmonary œdema fall into two groups.

(*a*) Those with definite venous engorgement. In these the face is congested, the lips blue, and the superficial veins of the face may be visibly distended. There is true hyperpnœa, *i.e.*, the breathing is not only increased in frequency but the actual amount of air reaching the lungs is greater than normal. The pulse is full and of good tension, and the rate is not often much above 100.

(*b*) Those with collapse. In these the face is pale and the lips of a leaden colour. The breathing is shallow, so that there is but little true hyperpnœa. The pulse is rapid (130 to 140) and weak.

In patients who recover, the œdema fluid is absorbed within a few days; in some cases signs of bronchitis or broncho-pneumonia, due to a secondary infection, persist for some time, but in most cases the lung returns to a condition which is normal except for the presence of some disruptive emphysema. In consequence, however, of the œdema of the lungs during the early stage, deficient oxygenation of the blood occurs, unless prevented by the administration of oxygen. The deficient oxygenation gives rise to wide-spread temporary injury in the various systems, leading to the general symptoms to be described later.

2. *Vesicants.*—The only one hitherto employed is dichlorethyl sulphide, an oily liquid used in shells, and scattered from them on the ground, where it slowly evaporates. This not only attacks those in the immediate vicinity of the shell-burst, but may also affect those who may walk over the contaminated ground later. The fluid may be spattered also on clothing, shell-casings, rifles, etc., and may thus become effective through direct contamination of the skin.

The main action of this group is an irritant one on the skin, eyes, and respiratory passages.

Special Symptoms. (*a*) *Early.*—These are insignificant, nothing being noticed immediately except a smell reminiscent of mustard, from which the gas derives its name (Mustard Gas). A soldier may not realise for many hours that he has been exposed to gas, until the more important delayed symptoms develop.

(*b*) *Delayed.*—These are the principal symptoms of this group and appear 3 to 24 hours after being gassed. They occur usually in the following order, and approximately after the intervals stated.

(i) Conjunctivitis. (3 hours.) This rapidly becomes very acute, and is accompanied by intense photophobia, and swelling of the lids, which may cause closure of the eyes for days.

(ii) Vomiting and epigastric pain. (4 to 8 hours.) These symptoms appear together as a rule, and are apt to be persistent and intractable.

(iii) Burns. (12 hours.) Wide-spread erythema with local vesication occurs going on to definite burns. The commonest sites are the axillæ, genitals, and back, but no area may be exempt. The affected surfaces frequently develop very marked pigmentation. Deep burns sometimes occur when the liquid itself comes into contact with the clothes or skin.

(iv) Laryngitis, pharyngitis, tracheitis and bronchitis (24–48 hours). These are the most dangerous symptoms. The degree and extent of the lesion may vary from a simple irritation of the surface to an ulceration of the mucous membrane of the whole passages, followed by infection of the raw surfaces. These conditions may be so extensive and severe as to cause death by themselves or in consequence of the development of broncho-pneumonia.

In a certain number of cases with severe involvement of the respiratory organs, which recover, there has evidently been some interference with the proper oxygenation of the blood, which may give rise eventually to symptoms resembling the after-effects of the suffocative gases as described below.

When a soldier is protected by the respirator the respiratory and eye symptoms are absent or slight.

Late Signs and Symptoms of Irritant Gas Poisoning.

These are the symptoms most commonly observed in the United Kingdom. The acute stage has subsided, and the patients are received on the average, about 14 days after being gassed. Depending on the action of the gas, these late symptoms will vary.

1. *General Symptoms.*—There is one group of symptoms which is more or less common to all forms of gas poisoning. These closely resemble those characteristic of "D.A.H." or the "Effort Syndrome," and commonly include dyspnœa, pain in chest, palpitation, dizziness and easy fatigue on exertion. The patient complains frequently of disturbed sleep, varying in degree. This may be characterised by dreams, paroxysms of coughing, starting awake with pressure on the chest, and even acute attacks of dyspnœa. Polycythæmia frequently occurs in association with these symptoms. There are also various nervous symptoms of a "functional" character, closely associated with this symptom-complex. In any given case, these symptoms may occur in varying degree.

The gas which is most productive of these symptoms is Phosgene. They occur very frequently after this form of gassing, and constitute by far the most important cause of discharge from the Army or reduction in category in those who have been gassed. These symptoms also follow "Mustard Gas," but are not as common nor as severe.

Treatment.—In patients exhibiting these general symptoms, *prolonged rest in bed is contra-indicated.* These patients should be

encouraged early to undertake increasing amounts of exercise. When practicable they should be placed on graduated physical exercises—mild ones at first, and gradually increasing in severity and duration. If this be not possible, the patients should be required to undertake definite amounts of walking, which should be increased in length and speed every few days until several miles at a fair marching pace are accomplished each day. Care should be taken that the exertion is not increased too rapidly. This may be determined by the condition of the patient at the end of the exercise. If there is obvious respiratory distress, which persists for more than a few minutes after the exercise is finished, or if the pulse-rate remains appreciably above the resting rate for more than five minutes, it may be judged that the exercise has been too severe. Also, the patient's subjective complaints must not be ignored, as they form a most valuable index to his condition. Præcordial pain, severe dyspnœa, giddiness or fatigue in an obvious degree, should be carefully avoided. *Patients who are making good progress should be returned as soon as possible to Army discipline;* the milder cases to their Regimental Depôts, and the moderate ones to a Command Depôt. *Prolonged stay in hospitals, either primary or auxiliary, is particularly apt, in these cases, to exaggerate the neurotic conditions, which are difficult to overcome.**

2. *Local Symptoms and Treatment.*—These are directly the result of the local action of the irritant gas on the skin, naso-pharynx, air passages, or eyes. These local lesions are most frequently the result of the vesicant type of gas (Mustard Gas). When the cases arrive in the United Kingdom, the acute stage is subsiding, and the after effects are to be dealt with.

(*a*) *Skin.*—"Burns" of varying degree may have occurred, and the treatment depends on their severity. The slighter ones heal perfectly satisfactorily under some non-irritating protective application such as Lassar's Paste. Severe burns are very intolerant even of mild applications, and extremely indolent of healing. If there be any sign of secondary infection, frequently repeated hot boric fomentations give great relief. If the burns are extensive, the dressings are very distressing. This may be relieved by hot alkaline baths, the patients being almost totally submerged. In a few minutes the dressings become soaked and will, as a rule, float off with little or no pain. The patients should be left in the bath for 20 minutes or half an hour. This promotes cleansing of the infected areas, and may be repeated two or three times a day, followed by Ambrene or liquid paraffin as protective dressings. In the later stages of healing, Lassar's Paste or mild boric ointment (*e.g.*, boric acid, gr. 15; powdered lead acetate, gr. 5; zinc oxide, gr. 20; unguentum paraffin, oz. 1) may be used.

For uncomplicated cases of erythema a dusting powder containing boric acid, starch, zinc oxide and chalk, may be applied freely,

* Recent experience of casualties from mustard gas in France has shown that the best results are obtained by vigorous measures at the outset for all except the very serious cases. Eye-shades are removed as soon as possible, and the men are not allowed to stay in bed for more than two or three days. They are sent out of doors early, and encouraged by discipline and exercises to forget that they have been gassed.

especially to susceptible regions such as the scrotum, groins and joint flexures. If secondary eczematisation has occurred without pyogenic infection, Lassar's Paste is usually effectual.

(*b*) *Eyes.*—The action of mustard gas is to produce an acute conjunctivitis (and, very rarely, keratitis). As a rule when the cases reach the United Kingdom this has become sub-acute. If there still are signs of acute inflammation the patient should be kept away from the light, and, if necessary, may wear dark glasses or a shade, but *it is most important that the use of these should not be continued beyond the inflammatory stage, otherwise functional photophobia is likely to result.* If pain is severe, hot fomentations over the eye-balls usually give relief. Liquid paraffin, which acts as a lubricant, and is absolutely non-irritating, should be instilled into the conjunctival sacs three times daily. When the inflammation has subsided, great benefit is obtained by the use of drops containing zinc sulphate, boric acid and adrenalin (zinc sulphate, gr. 1 to 2; boric acid, gr. 10; adrenalin solution, dr. 1; water, oz. 1). These drops should not be used just before the patient retires to bed.

Photophobia is a very constant and often persistent sequela, and is associated with marked blepharospasm. In the most persistent cases the functional element is clearly apparent, and the symptoms of the "Effort Syndrome" are frequently present in these patients. Cold douching—the patient plunging his head thrice daily into a basin of cold water—is found very effective in such cases; *every effort should be made to direct the patient's attention from the condition of his eyes by finding him constant employment, and by avoiding the use of eye shades and coloured glasses.*

A few patients aggravate the condition of the eyes by rubbing them. In these circumstances the conjunctiva of the lower lid will be found injected and swollen, while that of the upper lid is not. Possibly in some cases the rubbing of the eyes is deliberate, but in most cases it is of the nature of a functional "tic." Firmness and tact are required to deal satisfactorily with such patients.

(*c*) *The pharynx, larynx and main bronchi* may be similarly affected, producing an irritative inflammation with, at times, ulceration of a more or less extensive degree.

Nose.—The condition usually found when the patients arrive in the United Kingdom is a sub-acute inflammation. In a very few cases ulceration of an extensive degree may still persist. The orifices of the sinuses and nasal duct may be blocked by swelling, and the frontal headache so caused may persist for several weeks, the mucosa still showing an acute congestion.

Pharynx.—The mucosa shows irregular thickening, chiefly vertical, well within the lateral pharyngeal folds, and quite distinct from them. Small erosions of the surface epithelium may persist. The lateral pharyngeal folds and the anterior and posterior pillars are congested, but the main part affected is the posterior pharyngeal wall.

Larynx.—There is general redness and infiltration, especially on the arytenoid region, which extends up the aryteno-epiglottic folds. The vocal chords are reddened, but not acutely. The deficiency in

approximation is never great, and is due to paresis of the thyro-arytenoides internus, coupled with swelling of the tissues in the inter-arytenoid region.

Treatment.—For the throat and nose warm alkaline washes at least thrice daily are necessary.

The headache is relieved by inhalations of menthol (gr. 10 to 20 in 1 oz. of 60 per cent. spr. vini. rect., of which 1 dr. is added to a pint of hot water). Oil of peppermint—a few drops heated in a teaspoon and the vapour inhaled—has an equally good effect.

The laryngeal condition is best treated by inhalations of menthol, gr. 10., tinct. benzoin co. ad oz. 1, of which 1 dr. is added to a pint of steaming water. Tinct. benz. co. alone is not so efficacious.

When the infiltration has subsided, functional aphonia of varying degree is often present. This can be cured by breathing and articulation exercises, and a brisk rubbing of the posterior pharyngeal wall with the back of a laryngeal mirror.

Acute broncho-pneumonia is not infrequent while in France, but when the cases arrive in the United Kingdom, this is usually in the stage of convalescence. There may be a mild form of bronchitis present, which may or may not have been preceded by a broncho-pneumonia. In these cases the most distressing symptom is a troublesome hacking cough at night. This is best treated by inhalations as described under the laryngeal symptoms, and if necessary heroin should be given in $\frac{1}{8}$ grain doses for the relief of the cough. But the cough may persist out of all proportion to the extent of the physical signs, and may be to a great extent neurotic, and should be treated by suggestion and encouragement, as in the case of those exhibiting the functional aphonia and photophobia. In other cases the cough may be almost solely nocturnal, greatly disturbing sleep. This is undoubtedly closely associated with the general condition related to D.A.H., as described above.

Vomiting.—In a certain number of cases of gas poisoning vomiting may be a very persistent and troublesome symptom. There is no evidence that this is of an organic nature, but it seems undoubtedly to be neurotic. The patients who suffer from this as a rule remain well nourished. Examination of the stomach contents reveals a condition of hypochlorhydria, while the gastric motility remains unimpaired, as shown by a bismuth meal.

This condition is best treated by suggestion, and insistence that the condition is not serious. Twenty minims of dilute hydrochloric acid to an ounce of water after meals may be effectual. In more resistent cases fluid diet in small quantities frequently, with rest in bed and lavage, are usually sufficient. However, *the recurrence of the vomiting several months later make it important that its true neurotic nature should be recognised.*

Very rarely there is an indefinite history of hæmatemesis, which may raise a doubt as to the presence of gastric ulceration. In such cases this possibility must be carefully considered.

3. *Lachrymatory Group.*—No cases of pure lachrymatory gas poisoning are sent to the United Kingdom. Patients invalided for

other reasons than gas poisoning sometimes complain of having been exposed to these gases. It is, therefore, well to recognise that they have no after-effects.

As a rule it should not be necessary for a patient to be kept in hospital in the United Kingdom for more than 3 to 4 weeks. By this time he should be fit for the course of training given at a Command Depôt, or may even be returned to his Regimental Depôt for full duty. Some, of course, must remain much longer than others, and this is especially true of those suffering from extensive damage to the lungs during the early stage. Such cases as have persistent vomiting of the neurotic type and those suffering from severe symptoms of D.A.H. may also have to remain in hospital for a longer period, but they should not be kept in bed and should be made to undertake appropriate exercises and occupation. *The mild and moderate cases of all types do not, as a rule, require treatment in hospital for longer than one week to four weeks at the most.*

It is of importance at the present time to obtain statistics on the following points :—

(1) Disposal on discharge from hospital.
(2) Symptoms of gas poisoning which prolong the stay in hospital.
(3) In the case of patients who have been gassed being re-admitted to hospital, it is of great importance to determine what symptoms necessitate such re-admission, and if the gassing has had any influence on the production or perpetuation of them.

It is requested that this information be incorporated in the Medical Report on Army Form W. 3243 A.

Mine Gas Poisoning.

A small number of cases suffering from the after-effects of mine gas (CO) poisoning are evacuated to the United Kingdom. The history of the case clearly indicates these as a rule. A detailed description of the condition which results will be found in Memo. S.S. 308 : " Memorandum on Gas Poisoning in Mines."

The most important after-effects due to poisoning by Carbon Monoxide are similar to those described under the general symptoms (D.A.H. or " Effort Syndrome ") of lung irritant gases, and should be treated on the lines described above.

For official use only.

MEDICAL RESEARCH COMMITTEE.

Not Special Report Series

REPORTS

OF THE

CHEMICAL WARFARE MEDICAL COMMITTEE

No. 4. — POLYCYTHÆMIA AFTER GAS POISONING AND THE EFFECT OF OXYGEN ADMINISTRATION IN CHAMBERS IN THE TREATMENT OF CHRONIC CASES.

April, 1918.

In January, 1918, the Director-General, Army Medical Service, with the concurrence of the Controller of Chemical Warfare, appointed the following Committee to prepare reports, based upon information received from all sources at the Chemical Warfare Department, for submission to him with a view to their distribution to those concerned, to make suggestions for further co-ordinated medical investigations that may seem desirable, and to advise him generally in respect of the scientific medical aspects of Chemical Warfare :—

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REPORTS ALREADY PUBLISHED.

No. 1. Notes on the Pathology and Treatment of the effects of Pulmonary Irritant Gases. (*March*, 1918.)

No. 2. The Histological Effects produced by Gas Poisoning and their Significance. (*April*, 1918.)

No. 3. The Symptoms and Treatment of the late effects of Gas Poisoning. (*April*, 1918.)

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POLYCYTHÆMIA AFTER GAS POISONING AND THE EFFECT OF OXYGEN ADMINISTRATION IN CHAMBERS ON THE TREATMENT OF CHRONIC CASES.

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I.—ACUTE OLIGÆMIA AND SECONDARY POLYCYTHÆMIA AFTER GAS POISONING.

By Dorothy Dufton.

(*From the Physiological Laboratory, Cambridge.*)

May 21*st*, 1917.

Following out the suggestions contained in the memoranda dated G.H.Q. January 11th and January 24th, 1917, a large number of determinations have been made upon the number of red blood corpuscles and the amount of hæmoglobin per cubic millimetre of the blood at various periods after gassing. The animals used have been for the most part rabbits; in a few cases experiments have been carried out on goats. It has been found that an increase in the number of red blood corpuscles per cubic millimetre of the blood may take place within twenty minutes of gassing, and may still be observed in some cases for many weeks afterwards.

The following are typical cases:—

Table I.

Rabbit 13. Gas Chlorine 1/1,200, 30 mins.		Rabbit, G., 13. Gas Phosgene, 1/30,000, 30 mins.	
	Million per c.mm.		Million per c.mm.
Before gas	5.424	Before gas ...	5.600
20 mins. after ...	6.192	1 hour after ...	5.700
1 hour „ ...	6.912	2 hours „ ...	5.820
4 hours „ ...	6.196	5 „ „ ...	5.492
1 day „ ...	6.144	7 „ „ ...	5.736
2 days „ ...	6.176	1 day „ ...	6.776
3 „ „ ...	6.896	3 days „ ...	6.464
8 weeks „ ...	7.004	5 „ „ ...	5.977
		8 „ „ ...	6.455
		8 weeks „ ...	7.234

It will be seen that the increase in the number of red blood corpuscles consists really of two phenomena. The first, or early rise which takes place within a few hours of exposure to gas is a simple concentration of the blood, and will be referred to as acute oligæmia. Thus condition usually persists in a slightly diminishing degree for one or two days, and is then followed usually by a secondary rise, in this case a true polycythæmia, which may persist for many weeks.

Acute Oligæmia.—The condition of acute oligæmia has been investigated in the case of several gases and doses. The following table shows the gas and dose used, together with the maximum concentration observed and the time after gassing at which it took place. It must be borne in mind that in some cases the rabbits were killed as soon as a concentration was observed and that this may not have been the maximum obtainable.

TABLE II.

Rabbit, No.	Gas.	Concentration.	Time of Exposure.	Per cent. Increase in R.B.C.	Time, after Gas, of Maximum Increase.	Remarks.
Cl. 1 ...	Chlorine	1/3,000	15 mins.	29.5	7 hours	
,, 2 ...	,,	1/3,000	,,	41.5	8 ,,	
,, 3 ...	,,	1/3,000	,,	21.5	3 ,,	
,, 4 ...	,,	1/3,000	,,	Nil	—	
,, 5 ...	,,	1/3,000	,,	21.5	3 hours	
,, 6 ...	,,	1/3,000	,,	Nil	—	
,, 7 ...	,,	1/3,000	,,	25	3 hours	
,, 8 ...	,,	1/3,000	,,	14.6	4 ,,	
,, 9 ...	,,	1/1,300	20 mins.	7.3	1 day	
,, 10 ...	,,	1/1,300	,,	24.2	1 ,,	
,, 11 ...	,,	1/1,300	,,	Nil	—	Killed 4 hours before onset of œdema (?).
,, 12 ...	,,	1/1,200	30 mins.	28	20 mins.	Killed, 1 hour.
,, 13 ...	,,	1/1,200	,,	14.2	2½ hours	
,, 14 ...	,,	1/1,200	,,	15	1½ ,,	Killed, 2 hours.
G. 7 ...	Phosgene	1/32,000	,,	Nil	—	Killed, 4 hours.
,, 8 ...	,,	1/32,000	,,	15	4 hours	
,, 9 ...	,,	1/30,000	,,	33.5	7 ,, ...	Died, 7 hours.
,, 10 ...	,,	1/30,000	,,	Nil	—	Killed, 7½ hours before onset of œdema (?).
,, 11 ...	,,	1/30,000	,,	11.8	3 hours	
,, 12 ...	,,	1/30,000	,,	14	7 ,,	Killed, 7 hours.
,, 13 ...	,,	1/30,000	,,	22	1 day	
,, 14 ...	,,	1/30,000	,,	26	3 hours	Died, 3 hours.
,, 15 ...	,,	1/30,000	,,	17	3 ,,	Operated, 3 hours.
,, 16 ...	,,	1/15,000	15 mins.	29	4½ hours	
S. 11 ...	Chloropicrin	1/10,000	30 mins.	18.6	5 hours	
,, 12 ...	,,	1/5,000	15 mins.	13	7 ,,	

TABLE III.

Acute Oligæmia in Goats.

Gas Phosgene + Chloropicrin, 7th April.

Date.	Hb Determinations.		
	Goat 0.	Goat 2.	Goat 11.
April 7th, 1917 ...	54	64	47
,, 8th, 1917 ...	65	70	51
,, 10th, 1917 ...	58	70	Dead.

In a few cases, hæmoglobin determinations were carried out at the same time as the blood counts, and showed a proportional rise.

Example: Rabbit G. 13. Gas Phosgene 1/30,000, 30 mins.

Time—	Blood Count. Millions.	Hæmoglobin.
10 a.m.	5.600	74
Gas, 10.30–11	—	—
12...	5.700	—
1.45	5.800	—
6 p.m.	5.736	75
Next morning	6.776	82

The condition of acute oligæmia is thus due simply to loss of water from the blood causing a concentration of corpuscles. An experiment was carried out to estimate the amount of water lost by the blood in a typical concentration.

Rabbit G. 15 (weight 2.73 kilos) was gassed 1/30,000 phosgene for 30 mins. Its blood count before gas was 5.776 millions per cubic millimetre; three hours after gas it was 6,800, an increase of 17 per cent. At this stage the rabbit was anæsthetized with urethane, and the total blood volume determined by bleeding from the carotid into a known volume of distilled water, and by washing out the vessels with oxygenated Ringer's solution, giving artificial respiration. This experiment showed the total blood volume to be 142 c.c. The calculated blood volume before gassing would be $142 \times \frac{6.8}{5.7} = 163$ c.c.; a diminution in volume of 21 c.c. having therefore taken place.

In accounting for this diminution in volume, the first and most obvious factor to take into consideration is the pulmonary œdema. In a large number of cases, the animals were killed at short intervals after gassing, and it was found that in the great majority of cases, the amount of oligæmia bore a definite relationship to the amount of pulmonary œdema, as estimated by the macroscopic and microscopic appearance of the lungs. The greater the concentration, the greater degree of œdema.

As a more satisfactory way of measuring the degree of pulmonary œdema, we have made determinations of the heart-lung ratios of the animals used. In normal rabbits, the ratio of the weight of the lungs to the weight of the heart is about 1.5 : 1, and is very rarely greater than this. With the outpouring of fluid into the alveoli, the relative weight of the lungs increases, and ratios of lung weight to heart weight of 3.5 : 1 are not uncommon in severely gassed animals. That the lung-heart ratio is a fair test of the extent of pulmonary œdema is shown by the fact that the greater the ratio, the greater is the degree of œdema which is apparent both macroscopically and microscopically.

Table IV shows the relation between the percentage increase in the number of red blood corpuscles at the time of death, and the percentage increase in the lung-heart ratio. This increase is roughly estimated by supposing the normal weight of the lungs to be 1.5 times that of the heart.

TABLE IV.

Rabbit—	Per cent. Increase in R.B.C.	Per cent. Increase in Lung-heart Ratio.
G. 7	Nil	2.6
Cl. 11	Nil	6.6
G. 10	Nil	32
Cl. 9	7.3	20
„ 14	15	93.5
G. 8	15	120
Cl. 10	25	71.2
„ 12	28	80
G. 12	29	32
„ 9	33.5	148

A fairer comparison is that shown in Table V, where the percentage increase in the corpuscles at the time of greatest concentration is compared with the percentage increase in the heart-lung ratio.

TABLE V.

Rabbit—	Per cent. Increase in R.B.C. Maximum.	Per cent. Increase in Lung-heart Ratio.
Cl. 11	Nil	6.6
G. 7	4	26.5
„ 10	5.2	32
Cl. 9	7.3	20
G. 8	15	120
Cl. 14	17	93.5
„ 10	25	71.2
„ 12	28	80
G. 12	29	32
„ 9	33.5	148

The relationship is by no means constant, but, taking into consideration the errors involved in both measurements, it may be stated in general terms that the greater the concentration of the blood the greater is likely to be the amount of pulmonary œdema. That there are other factors besides the pulmonary œdema which contribute to the condition of oligæmia is shown by correlating the blood-volume experiment with the lung-heart ratio determinations. Taking a severe case of œdema, fatal within 6 hours after phosgene poisoning, the weights of the heart and of the lungs respectively were 6.3 gm. and 23.1 gm. Assuming the weight of the lungs in the normal state would be, roughly speaking, 9.5 gm., we can account for an outpouring of about 13 c.c. of fluid into the lung. In most cases the calculated volume of liquid entering the lung is 9 or 10 c.c. But the blood-volume experiment gave us a diminution in volume of 21 c.c. to account for, and we must therefore consider the other factors which may be at work.

In the first place we may have the effect of shock. Dale and Laidlaw[1] have found that in cases of surgical shock there may be a great concentration of the blood, probably due to a generalized tissue œdema. Bainbridge and Trevan[1] have correlated this with the fact noted by Elliott, Cannon, and others, " that extreme emotion

[1] Memorandum upon Surgical Shock and Some Allied Conditions. Medical Research Committee, 1917.

or pain, which are factors in some cases of shock, are accompanied by an outpouring of adrenaline from the suprarenal glands." They have found that intravenous injection of adrenaline causes an immediate oligæmia.

As a third possible factor, in this case dependent on the damaged condition of the lung, we may have the general tissue œdema, brought about by the increased osmotic pressure of the tissues caused by oxygen want (*see* Fletcher[1]). If this factor has any serious effect, it might be supposed that exposure of the animal to an atmosphere containing a high percentage of oxygen immediately after gassing would reduce the degree of oligæmia. Up to the present only one such experiment has been carried out. Rabbit G. 17 was gassed 1/30,000 phosgene for 30 minutes, and after twenty-four hours, the observed concentration was 14 per cent. This concentration is smaller than would be expected, but much more data are necessary before any general statement can be made.

A fourth factor may be the outflow of fluid into the alimentary canal (*see* reports from Porton and reports on cases of gas poisoning).

Chronic Polycythæmia.—We shall now turn to the investigations of the secondary increase in the number of blood corpuscles. We regard this as the phenomenon observed by Price-Jones and Hunt in convalescent gassed cases. This however is clearly not a case of simple oligæmia, since the number of corpuscles goes up in advance of the hæmoglobin.

Example. Rabbit G. 13. Gas Phosgene 1/30,000 for 30 mins.

Time—	Blood Count. Millions.	Hæmoglobinometer
Before gas	5.600	74
1 hour after	5.700	—
7 hours „	5.786	75
1 day „	6.776	82
3 days „	6.464	81
5 „ „	6.080	—
7 „ „	5.784	79
9 „ „	6.548	79

(Onset of true polycythæmia.)

This secondary or true polycythæmia may pass off in a few days, but it has been found to persist in three cases in which determinations were made eight weeks after gassing. In two of these cases the animals were subsequently killed, and the sections of the lung revealed in one case marked thickening of the alveolar walls, and in the other case stripping of the epithelium and emphysema. In neither case was there any trace of pulmonary œdema.

These observations lead us to suppose that the polycythæmia is caused by a definite stimulus to the bone marrow due to imperfect ventilation through the lungs. In the case of the polycythæmic rabbit whose lung showed stripping of the epithelium and emphysema, the

[1] W. M. Fletcher. *Journal of Physiology*, 1903, **30**, 414.

phenomenon may be due to decreased volume of the blood[1]. It is a well-known fact that oxygen want gives rise to polycythæmia. This phenomenon has been noted at high altitudes by Zuntz and his co-workers[2], and by the members of the Pike's Peak Expedition[3], and in the case of aviators by Meyer and Seyderhelm[4], and has been induced experimentally by Kolls and Loevenhart[5], who found an increase in the red blood corpuscles and in the hæmoglobin of rabbits after three days in a chamber, the atmosphere of which contained 12 per cent. of oxygen.

Experimental polycythæmia has also been induced by exposure of rabbits to atmospheres containing 3–4 per cent. of carbon dioxide. As for example, the following are the blood counts of a rabbit which for four days lived in an atmosphere containing about 4 per cent. 4 CO_2:—

—	Before	In CO_2.				In Air.	
		1st day.	2nd day.	3rd day.	4th day.	1st day.	2nd day.
Red corpuscles	5.95	6.49	6.46	6.83	7.13	7.16	5.98
(Millions per c.mm.) ...	6.11	6.49	6.72	6.92	7.14	6.97	6.15

It seems probable that the whole phenomenon of polycythæmia is due to an increase of the hydrogen ion concentration of the blood, a condition which may be induced either by oxygen want or by excess of acid.

To find out whether or not oxygen want was the determining factor in the occurrence of polycythæmia in gassed patients, convalescent animals which showed an abnormally high blood count have been subjected to an atmosphere containing a high percentage of oxygen. The experiments have been carried out in a glass chamber measuring 9 ft. × 6 ft. × 6 ft. The oxygen was let in from cylinders, and the carbon dioxide and water absorbed by means of a soda-lime scrubber.

[1] Barcroft. Report to Royal Society on delayed Phosgene Poisoning. April, 1916.

[2] Zuntz, Loewy, Müller and Caspari. Höhenklima und Bergwanderungen. Berlin, 1906.

[3] Douglas, Haldane, Henderson and Schneider. *Phil. Trans. Roy. Soc.*, B. **103**, 18.
Barcroft. Respiratory Function of the Blood. Cambridge, 1913, p. 120.

[4] Uber Blutuntersuchungen bei Flieger. Meyer and Seyderhelm, *Deutsch. Med. Woch*, 1916, **42**, 1245–1247.

[5] Kolls and Loevenhart. *Journal of Biological Chemistry*, 1914, **17**, xxxviii.

The air was circulated by an electric fan. The following table shows some of the typical results obtained :—

Rabbit G. 16. Gas Phosgene 1/15,000 for 15 min.

Date.	Atmosphere.	Blood Count.	Hæmoglobin.
1917.		Millions.	
April 23rd (before gas) ...	Air	4.898	—
„ 23rd (4½ hours after) ...	„	6.700	—
„ 25th	„	6.296	—
May 9th (put in oxygen) ...	„	6.800	—
„ 10th	30 per cent. O_2	5.594	—
„ 11th	„	4.756	—
„ 12th (taken out)	„	4.788	60
„ 13th	Air	5.752	61
„ 14th	„	5.808	60
„ 16th	„	5.880	62

Rabbit Cl. 13. Gas Chlorine 1/1,200, 30 min.

Date.	Atmosphere.	Blood Count.	Hæmoglobin.
1917.		Millions.	
February 21st (before gas) ...	Air	5.424	—
„ 21st (maximum concentration)	„	6.219	—
February 22nd	„	6.144	—
„ 23rd	„	6.176	—
„ 24th	„	6.896	—
May 4th (taken into chamber)	„	7.004	—
„ 5th	30 per cent. O_2	6.921	—
„ 7th	„	6.147	—
„ 9th (taken out)	37 per cent. O_2	5.696	—
„ 10th	Air	6.864	—
„ 11th	„	6.928	—
„ 12th (put in chamber) ...	„	6.944	60
„ 13th	37 per cent. O_2	6.036	59
„ 15th	„	5.504	60
„ 16th	„	5.600	55
„ 18th	„	5.460	58

In one case a rabbit was put into the oxygen chamber immediately after gassing, with the following results :—

Rabbit G. 19. Gas Phosgene 1/32,000 for 30 mins. (May 12th, 1917, 5.47 p.m. to 6.17 p.m.). Put into chamber 6.20 p.m., May 12th, 1917.

Date.	Blood Count.	Hæmatocrit.	Hæmoglobin.
1917	Millions.		
May 12th (before gas) ...	6.864	42	72
„ 13th	7.824	49	78
„ 14th	6.736	40	72
„ 15th	6.596	40	72
„ 16th	6.724	42	65
„ 17th	6.720	—	68
„ 18th	6.608	41	69
Taken out of oxygen 11.30 a.m., May 18th, 1917.			
May 19th	7.088	—	69
„ 21st	7.344	45	73

The conclusion from these experiments is that the chronic polycythæmia is caused by oxygen want, and can be temporarily abolished by placing the animal in such an atmosphere that the imperfect oxidation of the blood due to the damaged condition of the lung is corrected.

Experiments are now being carried out to find out whether diet has an effect on the hæmoglobin value in cases of chronic and of experimental polycythæmia. In the case of polycythæmia induced by exposure to an atmosphere containing a high percentage of carbon dioxide, it was found that the rabbits, which were being fed on swede turnips, bran and oats, shewed no increase in the hæmoglobin value.

For example :

—	Before Exposure.	After 4 days in air containing 3–4 per cent. CO_2.	2 days after internment.
Red blood corpuscles	4.18	6.00	4.50
Hb meter	60	61	57.0
	11.1	11.3	10.3
Oxygen capacity (ferri-cyanide) ...	10.1	11.2	10.0

At the suggestion of Captain C. G. Douglas, M.C., R.A.M.C., the experiments were continued on rabbits which were fed for the most part on fresh green cabbage. In this case there was a rise in the hæmoglobin value comparable with, but somewhat later than, the rise in the number of red blood corpuscles.

For example :—

—	Before internment (green food and 3–4 per cent. CO_2 begin).	3 days.	6 days.	11 days.
Red corpuscles	4.580	5.200	7.220	7.264
Hb meter	76	80	85	91

There is an indication that a similar result can be obtained in the case of polycythæmia produced by gas poisoning, thus :—

Rabbit Cl. 13. Gassed Chlorine 1/1,200, February 31st, 1917.			Rabbit G. 17. Gas Phosgene. May 12th, 1917. 1/32,000, 30 min.		
Date.	Blood Count.	Hb.	Date.	Blood Count.	Hb.
1917.			1917.		
February 21st (before gas)	5.424	—	May 12th } in oxygen	6.864	72
May 4th	7.004	—	„ 13th } in oxygen	7.824	78
„ 9th (after 4 days in O_2)	5.696	—	„ 14th } in oxygen	6.736	72
May 12th (after 3 days in air)	6.944	60	„ 17th } in oxygen	6.720	68
May 18th (after 5 days in O_2)	5.460	58	„ 19th (after 1 day in air)	7.088	69
May 21st (after 3 days in air)	7.088	77	May 21st (after 3 days in air)	7.344	73
From May 18th, 1917, onwards the rabbit was given large quantities of green food.			The rabbit was given no green food throughout the experiment.		

Further experiments along these lines, together with control experiments, are to be carried out.

II.—THE TREATMENT OF CHRONIC CASES OF GAS POISONING BY CONTINUOUS OXYGEN ADMINISTRATION IN CHAMBERS.[1]

By J. Barcroft, G. H. Hunt, Capt. R.A.M.C., T.F., and Dorothy Dufton.

(*From the Porton and Cambridge Physiological Laboratories.*)

Introduction.

The treatment of chronic gassed patients by the administration of oxygen was suggested by the possible interpretation of the symptoms they exhibit. The symptoms to which our attention was especially drawn were :—

(1) Disordered action of the heart.
(2) Nocturnal dyspnœa.
(3) High red blood counts (polycythæmia).
(4) Low percentage of CO_2 in alveolar air.
(5) Acidosis and kindred conditions.

A single case may not show all these symptoms to the same degree. Indeed, in the report by Hunt and Price Jones,[2] which drew attention to polycythæmia as an obvious feature of chronic cases, the cases which they observed were classified into: (1) those in which polycythæmia and nocturnal dyspnœa were conspicuous, and (2) those in which disordered action of the heart was most prominent. Between these extreme types there were intermediate cases showing symptoms common to each group.

Douglas[3] examined the alveolar air in a number of Hunt and Price Jones' cases, and found an abnormally low CO_2 pressure in many of them—a research which is not quite simple of interpretation owing to uncertainty as to whether the alveolar air of gassed patients can be regarded as of uniform composition.[4]

Sleeplessness, neurasthenia and nocturnal dyspnœa have been described as leading symptoms of patients who had suffered from chronic gas poisoning in the filling factories,[5] associated often with breathlessness on exercise and disordered action of the heart.

Acidosis has been observed in gassed cases of the severer type at Boulogne[6] after the gas attacks in April, May and June, 1915, and also in cases sent to the Military Hospital at Hampstead[7] for investigation. Acidosis on exercise has also been observed in gassed animals.[8]

The fundamental idea on which our treatment is based is that the whole train of symptoms shown by these patients is the same as that

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[1] The chambers consisted of three rooms of capacity of 10, 10 and 12 cubic metres respectively made of plate glass in iron frames and fitted with the necessary scrubbers for the removal of CO_2 and aqueous vapour.

[2] Hunt and Price Jones. *Report forwarded to G.H.Q., France.*

[3] Douglas.

[4] Haldane, Meakins and Priestley's *C.W.M.C. Report.* No. 5. (*In the Press.*)

[5] Shufflebotham. *C.W.M.C. Report.* No. 1.

[6] Barcroft. *C.W.M.C. Report.* No. 6. (*In the Press.*)

[7] Barcroft, Lewis and others, as yet unpublished.

[8] Barcroft and others. *C.W.M.C. Report.* No. 6. (*In the Press.*)

exhibited by dwellers at high altitudes. Among such the occurrence of sleeplessness, nocturnal attacks of breathlessness and rapidity of the pulse after exercise is common, and polycythæmia is now beyond doubt.[1] Acidosis,[2] expecially in exercise, has been observed as a well-marked phenomenon as well as its complement lowered CO_2 pressure in the alveolar air. It is true that at high altitudes not all of these symptoms occur in an equal degree in every person and in this there is a marked resemblance to the effect of gas poisoning.

As rarefied air or, more precisely, insufficient available oxygen, is undoubtedly the cause of the trouble at high altitudes, it seemed reasonable to try the effect of a greater concentration of oxygen than these gassed patients were obtaining in ordinary air.

Having obtained this suggestion, a method of treatment was worked out with rabbits at Cambridge. In these animals a chronic condition of polycythæmia was easily produced by exposure to chlorine or phosgene, and it was as easily abolished when the animals were placed in chambers containing 35–40 per cent. of oxygen.[3]

This result having been obtained, there seemed to be sufficient justification for the application of the same treatment to man.

Account of typical Experiments made to Investigate the Influence of an Atmosphere containing 40 per cent. Oxygen on a Patient suffering from the Later Effects of Gas Poisoning.

Case 1.—*D.*

The patient, aged 47, was a bricklayer's labourer by occupation. Previous to being gassed he was an exceptionally healthy man; he had not had any serious illness, and was able to do 12–14 hours' heavy work a day without any feeling of fatigue. For the last 18 months he had worked in a gas factory where chloropicrin was made. He had often been exposed to small quantities of gas, but not in sufficient strength to cause any marked symptoms. On June 25th, 1916, he was severely gassed; the immediate symptoms were dryness of the throat, nausea, vomiting, cough, pain and tightness of the chest and dyspnœa; he was not unconscious. Since that time he has suffered from headaches, muscular pain and dyspnœa on exertion as well as "asthma" at night. The asthmatic attacks usually begin after he has been coughing; he has a feeling of suffocation, shortness of breath, and a "heavy aching" over the front of the chest; he finds that sitting up in bed or going to an open window affords some relief. The attacks occur every night, sometimes twice in one night, and may persist for as long as three hours; they seriously disturb his rest, and he often does not sleep more than two hours a night. (These attacks seem to be typical of those described by Hunt and Price Jones.)

On examination he was a healthy-looking, rather thin man. His

[1] Literature in Report on Pike's Peak observations. *Phil. Trans. Roy. Soc.*, B 2, **203**, 185.

[2] Report of Monte Rosa Expedition. *Phil. Trans. Roy. Soc.*, B, **206**, 49. Also *Journ. Physiology*, 1911, **42**, 44.

[3] D. Dufton. Report on Acute Oligæmia (*see Part I of this Report*).

pulse was 76, and of normal volume and tension. Occasionally a sibilant rhonchus, which disappeared on coughing, was heard in the chest, but otherwise the lungs appeared healthy. Nothing abnormal was found in the heart, nervous system or abdomen; the urine was normal. An X-ray examination of the chest made by Dr. Scales showed nothing obviously abnormal. The red blood cells were increased in number to 6,100,000; the hæmoglobin was 102 per cent.

The effect of exercise was tested by making him walk up and down 4 flights of stairs 3 times in 4 minutes. (This was a severe test.) On completion of the exercise he was extremely dyspnœic, and his pulse rate only returned to normal[1] after 25 minutes. (See Table 1.) In a control of about the same age the pulse after the same exercise fell to normal in 13 minutes, and the dyspnœa was much less. (See Table 2.)

TABLE 1.—Effect on pulse rate of walking up 4 flights of stairs 3 times in 4 minutes *before treatment*. Pulse before exercise, 76.

Pulse after Exercise.

Time.	Rate per Minute.	Time.	Rate per Minute.	Time.	Rate per Minute.
1st ½-minute ...	156	3rd minute ...	108	13th minute ...	96
2nd „ ...	136	4th „ ...	106	14th „ ...	96
3rd „ ...	132	5th „ ...	104	15th „ ...	96
4th „ ...	116	6th „ ...	102	20th „ ...	92
5th „ ...	112	7th „ ...	102	25th „ ...	84
6th „ ...	100	8th „ ...	100	32nd „ ...	**82**
7th „ ...	116	9th „ ...	96	35th „ ...	82
8th „ ...	112	10th „ ...	96	42nd „ ...	78
		11th „ ...	98	45th „ ...	76
		12th „ ...	96	47th „ ...	74

TABLE 2.—Effect on pulse rate of walking up 4 flights of stairs 3 times in 4 minutes on a normal subject of about the same age as the patient. Pulse before exercise, 72.

Pulse after Exercise.

Time.	Rate per Minute.	Time.	Rate per Minute.	Time.	Rate per Minute.
1st ½-minute ...	108	3rd minute ...	86	11th minute ...	80
2nd „ ...	104	4th „ ...	84	12th „ ...	82
3rd „ ...	96	5th „ ...	88	13th „ ...	78
4th „ ...	92	6th „ ...	82	14th „ ...	**78**
5th „ ...	92	7th „ ...	84	16th „ ...	78
6th „ ...	88	8th „ ...	82	17th „ ...	76
7th „ ...	88	9th „ ...	82		
8th „ ...	88	10th „ ...	80		

[1] The test consists essentially in determining the length of time which elapses before the pulse returns to within six beats of its resting rate. The period at which this happens is marked in heavy type in all the pulse-rate tables.

At 11 p.m. on July 24th, he was put into a chamber of 22 cubic metre capacity containing 40 per cent. oxygen, and was kept in it for the following four days and nights, except for 2–3 hours during each day, when he went out for exercise. (See Tables 10 and 11.)

TABLE 3.—Effect on pulse rate of walking up 4 flights of stairs in 4 minutes 10 seconds, *after treatment* (day of cessation). Pulse before exercise, 90.

	Pulse after Exercise.					
Time.	Rate per Minute.	Time.	Rate per Minute.	Time.	Rate per Minute.
1st ¼-minute ...	160	3rd minute ...	108	14th minute ...	96
2nd ,, ...	132	4th ,, ...	104	16th ,, ...	96
3rd ,, ...	116	5th ,, ...	98	17th ,, ...	96
4th ,, ...	112	6th ,, ...	**96**	18th ,, ...	96
5th ,, ...	124	7th ,, ...	96	19th ,, ...	96
6th ,, ...	116	8th ,, ...	98	20th ,, ...	94
7th ,, ...	112	9th ,, ...	98		
8th ,, ...	103	11th ,, ...	98		

Table 4 shows the changes in numbers of red cells and hæmoglobin percentage that were observed at different periods.

TABLE 4.

First Internment (*July 24th–28th*).

Date.	Time.	Red Cells.	Hb.
1917.		Millions per cub. mm.	Per cent.
July 24th	6 p.m.	6.10	102
,, 25th	10 a.m.	6.10	102
	6 p.m.	5.92	101.5
,, 26th	10 a.m.	5.31	97
	6 p.m.	5.42	96
,, 27th	10 a.m.	5.18	96
	6 p.m.	5.02	94
,, 28th	10 a.m.	4.96	94
	6 p.m.	4.90	94
,, 29th	10 a.m.	4.96	94
	6 p.m.	5.04	96
,, 30th	10 a.m.	5.21	96.5
Aug. 2nd	—	5.40	101.5
,, 9th	—	5.10	101
,, 29th	—	5.45	102

Tables 5, 6 and 7 show effect of exercise at different stages of treatment upon pulse rate.

TABLE 5.—Effect on pulse rate *before treatment* of lifting a pail of water 21 times in 1 minute 35 seconds. Pulse before exercise, 86.

Pulse after Exercise.	Rate per Minute.
1st ¼-minute	136
2nd „	128
3rd „	120
4th „	112
5th „	108
6th „	104
7th „	**92**
8th „	92

TABLE 6.—Effect on pulse rate of lifting a pail of water 21 times in 1 minute 30 seconds, *while patient was inside the chamber*, at 1.30 p.m., on July 27th, *i.e.*, the third day after treatment was begun. Pulse before exercise, 74.

Pulse after Exercise.	Rate per Minute.
1st ¼-minute	116
2nd „	100
3rd „	100
4th „	**80**
5th „	80
6th „	72
7th „	72
8th „	72

TABLE 7.—Effect on pulse rate of lifting a pail of water 21 times in 1 minute 35 seconds, *after treatment* was over, and while the patient was outside the chamber. Pulse before exercise, 82.

Pulse after Exercise.	Rate per Minute.
1st ¼-minute	128
2nd „	104
3rd „	96
4th „	92
5th „	**84**
6th „	76
7th „	76
8th „	80

At 10 p.m. on July 28th, he was taken out of the chamber and passed the remainder of the time, during which he was under observation, in the ordinary air. On the nights of July 28th and 29th he slept quite as well as he did in the chamber.

On August 4th his general improvement was maintained, he had had no attacks of asthma, and had slept well at night. The improvement in walking continued and examination of the chest showed nothing abnormal.

On August 9th (12 days after cessation of treatment), the patient stated that he was still sleeping well and was able to undertake more exercise. His general condition appeared to have improved, and there had been no chest symptoms beyond a slight cough. An examination of the blood was made and the hæmoglobin was 101 per cent. while the red cell counts as a result of two examinations were 5.016 million and 5.090 million respectively, giving an average of 5.053 million, the colour index being 1.

Table 8 shows the effect on the pulse rate of walking up and down 4 flights of stairs in 3 minutes and Table 9 shows the effect of the same exercise on a healthy subject of about the same age as the patient. In the case of the patient the pulse rate returned to normal in 12 minutes while in the control subject it returned to normal in 8 minutes.

TABLE 8.—Effect on pulse rate of walking up and down 4 flights of stairs twice in 3 minutes *after treatment*. Pulse before exercise, 92.

Pulse after Exercise.

Time.	Rate per Minute.	Time.	Rate per Minute.
1st ½-minute	156	3rd minute	116
2nd ,, ...	140	4th ,, ...	104
3rd ,, ...	128	5th ,, ...	108
4th ,, ...	116	6th ,, ...	108
5th ,, ...	124	7th ,, ...	104
6th ,, ...	124	8th ,, ...	100
7th ,, ...	120	9th ,, ...	**98**
8th ,, ...	112	10th ,, ...	100
		11th ,, ...	100
		12th ,, ...	96

TABLE 9.—Effect on pulse rate of same exercise as in Table 8 on healthy subject and about same age. Pulse before exercise, 74.

Pulse after Exercise.

Time.	Rate per Minute.	Time.	Rate per Minute.
1st ½-minute	144	3rd minute	92
2nd ,, ...	124	4th ,, ...	82
3rd ,, ...	112	5th ,, ...	82
4th ,, ...	104	6th ,, ...	**80**
5th ,, ...	104	7th ,, ...	80
6th ,, ...	96	8th ,, ...	78
7th ,, ...	92		
8th ,, ...	88		

TABLE 10.—Composition of air in the chamber, and hours at which oxygen was put in.

Date.	Hour.	Oxygen.	CO_2.
		Per cent.	Per cent.
July 24th	11.15 p.m.	40	0.0
„ 25th	9.45 a.m.	35	0.2
„ 25th	1.15 p.m.	32.7	0.0
„ 25th	2.0 p.m.	—*	—
„ 25th	2.30 p.m.	35.6	0.1
„ 25th	10.0 p.m.	—†	—
„ 25th	10.15 p.m.	44.6	0.2
„ 26th	11.0 a.m.	38.4	0.1
„ 26th	2.0 p.m.	36.6	0.15
„ 26th	8.45 p.m.	33.1	0.2
„ 26th	9.0 p.m.	—†	—
„ 26th	10.15 p.m.	40	0.2
„ 27th	9.15 a.m.	37.5	0.3
„ 27th	10.0 p.m.	—†	—
„ 27th	11.0 p.m.	40	0.14
„ 28th	11.0 a.m.	37	0.2
„ 28th	2.0 p.m.	35.5	0.2

* Two cylinders of oxygen put into chamber.
† Three cylinders of oxygen put into chamber.

TABLE 11.—Times during which patient was in and out of chamber.

July 24th.—11.15 p.m. Entered chamber, slept from 11.45 p.m. till 4.15 a.m.; awakened by cough, also complained of headache; headache disappeared when CO_2 was removed. Slept from 4.15 to 7.40. Patient had no attack of asthma, and said he had had the best night's rest since he was gassed.

July 25th.—In the chamber all day; quite comfortable. Slept from 11.50 p.m. till 4 a.m. Awake from 4 a.m. till 4.15, some cough, but no asthma. Slept from 4.15 till 6 a.m., and from 6.10 a.m. till 8.15. Dozed from 8.15 till 9.45.

July 26th.—In chamber all day except between 12 noon to 1.30 p.m. and 6 to 7 p.m. when he went for a walk. Slept for 1¾ hours during the afternoon. At night slept from 10.30 to 12.30 and from 1 to 3 a.m.; awake (coughing) from 12.30 to 1 a.m. and from 3 to 3.15. Slept from 3.15 to 7.15. Dozed from 7.15 to 8.30.

July 27th.—Out walking from 9.30 to 12, and from 6.30 to 8 p.m., but spent the rest of the day in the chamber. At night slept from 11.45 to 4.15 and from 4.30 to 7.45. Coughed from 4.15 to 4.30.

July 28th.—Out walking from 12 to 1 p.m. and from 6 to 7.30 p.m., but passed the rest of the day in the chamber. Slept for two hours in the afternoon. Came out of the chamber at 8.30 p.m. after being under oxygen treatment for 84½ hours altogether. He slept in the ordinary air, and was rather restless at first, but slept on and off from 11.30 till 5 a.m. Coughing from 5 to 5.30. Slept from 5.30 to 7 a.m.

July 29th.—Spent the day walking about outside, or reading in the laboratory. Slept in the ordinary air and passed a good night except for occasional coughing. No attack of asthma.

The effects of the treatment may be summarised as follows :—

1. He did not have a single asthmatic attack at night, but slept extremely well, usually for 6–8 hours, only being occasionally awakened by coughing.
2. He was able to walk much faster, and without any dyspnœa ; when the same stair test was repeated at the end of the treatment, the dyspnœa was much less, and the pulse rate returned to normal in 12 minutes. (See Table 8.)
3. The hæmoglobin fell from 102 per cent. to 94 per cent., and the red cells from 6.100 million to 4.690 million.
4. The degree of acidosis was reduced. The buffer salts showed no change.
5. The patient stated that he felt much better, and was enthusiastic about the results of the treatment.

Second Period of Internment.

His improvement was maintained until August 23rd, when the dyspnœa at night returned, and he noticed that he was becoming short of breath again on exertion. When tested on August 29th, his response to exercise was not so good. This relapse is to be ascribed to two causes: (1) between August 21st and August 25th he did 35 hours very heavy work without any previous training and against advice ; (2) on August 25th he was again " gassed."

In spite of this he felt very much better than before treatment, and his attacks at night were of shorter duration and less frequent than formerly.

He was re-examined on October 29th. After a test exercise (4 flights of stairs in 1 minute 5 seconds), his pulse fell to within 8 beats of its original rate in 13 minutes. His red cell count was 5.95 million, and his hæmoglobin 103.5 per cent. (See Tables 12 and 13.)

Treatment.

He was put in the chamber on October 29th, at 11.30 p.m., and remained there, with intervals for exercise, until 10 a.m. on November 2nd. The concentration of oxygen in the chamber is shown in Fig. 15. His red cell count fell much more quickly than on the previous occasion, and reached 5.14 million in less than 24 hours, and at the conclusion of the treatment was 5.19 with a hæmoglobin of 100 per cent. (See Table 13.) His dyspnœa on exertion was much diminished, and after the test exercise his pulse fell rapidly. (See Table 12.) He felt much better, and his attacks of dyspnœa at night stopped entirely. On November 29th, without further internment, the hæmoglobin was 90 and the corpuscles 4.5 million.

TABLE 12.—Pulse rate after exercise.

Before Second Treatment (*October 29th*, 1917).

Time.	Rate per Minute.	Time.	Rate per Minute.	Time.	Rate per Minute.
Normal ...	64	3rd minute ...	84	14th minute ...	74
1st ¼-min. ...	—	4th „ ...	84	15th „ ...	76
2nd „ ...	—	5th „ ...	80	16th „ ...	76
3rd „ ...	120	6th „ ...	80	17th „ ...	74
4th „ ...	104	7th „ ...	84	18th „ ...	78
5th „ ...	80	8th „ ...	78	20th „ ...	72
6th „ ...	80	9th „ ...	78	21st „ ...	76
7th „ ...	84	10th „ ...	80		
8th „ ...	84	13th „ ...	72		

After Second Treatment (*November 1st*, 1917).

	Rate per minute.
Normal	78
1st ¼-minute	—
2nd „	—
3rd „	108
4th „	88
5th „	**72**
6th „	72
7th „	72

TABLE 13.

—	—	Red Cells	Hb.
		in Millions.	per cent.
October 29th	6 p.m.	5.95	103.5
	11.30 p.m. (entered chamber)		
„ 30th	Noon	5.67	103
	10 p.m.	5.14	102.5
„ 31st	10 a.m.	5.18	101
	6 p.m.	4.55	100
November 1st	10 a.m. (left chamber)	5.19	100
„ 29th ...	—	4.54	90

TABLE 14.—Case 1. *D.* Blood Counts and Hæmoglobin Values.

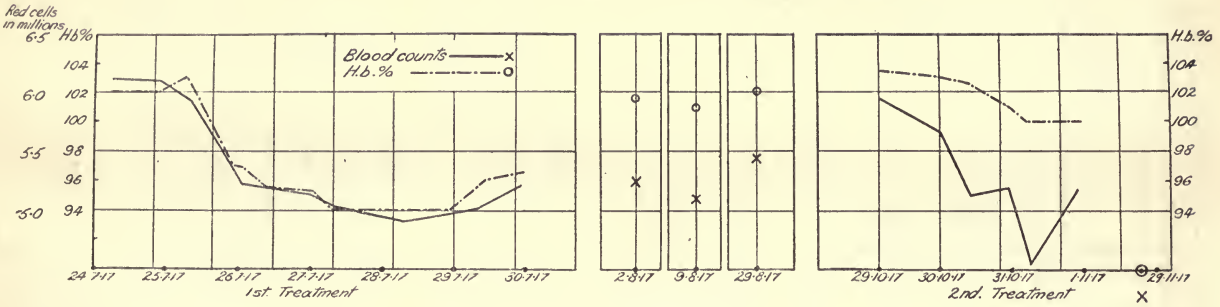
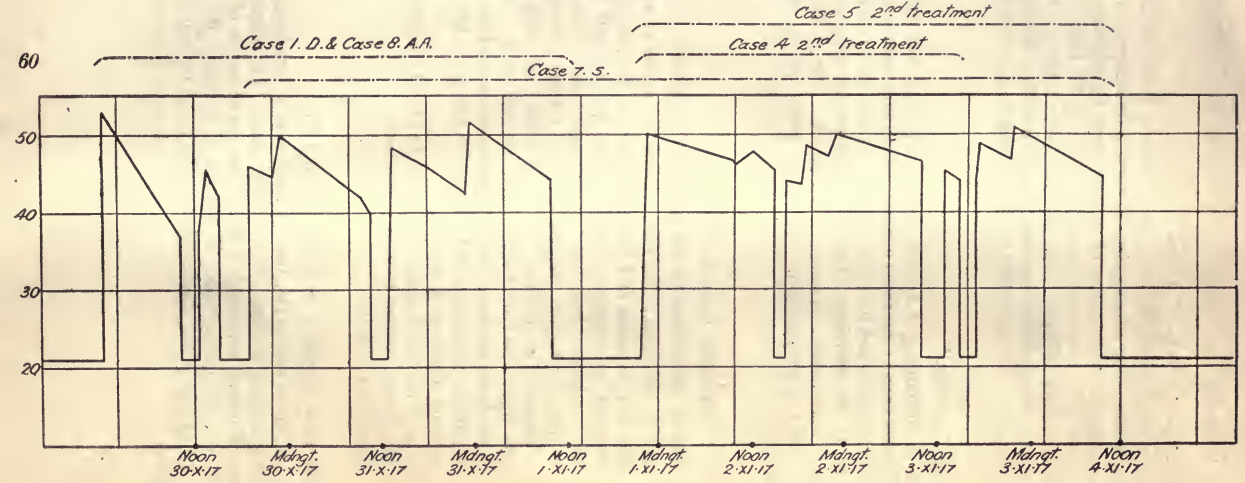


TABLE 15.—Oxygen percentage.



CASE 2.—*T. J. Age* 37. *Poisoning by Chloropicrin.*

History previous to being "gassed."

The patient has always been a very healthy man, and accustomed to heavy work. For some years he was a bricklayer; in 1908 he became a traveller for a firm of drapers, and this involved walking several miles a day carrying samples weighing 50 lbs. He entered a munition factory in April, 1916, and for 3–4 months did very heavy work without any difficulty or shortness of breath. He used to play football regularly, but gave this up in 1912, as he had not time for it.

History of "gassing."

From the beginning of August, 1916, the patient was often exposed to small doses of gas; on three occasions the symptoms were sufficient to necessitate rest in bed for two to three days, but on no single occasion were they at all alarming. The usual symptoms immediately after "gassing" were cough, dyspnœa, pain all over the chest, vomiting, headache and lachrymation. He was often giddy, but never unconscious.

Symptoms subsequent to being "gassed."

The patient complained of the following symptoms:—

1. Pain in the throat and chest: this comes on at any time of the day or night, and has no relation to exercise or to meals.
2. Dyspnœa on exertion: he states that he can walk half a mile in 15 minutes, but that a faster pace causes discomfort.
3. Dyspnœa at night: this comes on in attacks, which are quite spasmodic in nature; he has a feeling of suffocation, and sits up in bed or walks about to get relief. The attacks last about an hour; they sometimes occur for four or five nights in succession, but he may be free from them for three or four nights at a stretch.
4. Cough: this is not severe, and he only has a little expectoration. He is very subject to cold in the head.
   Digestion is good.

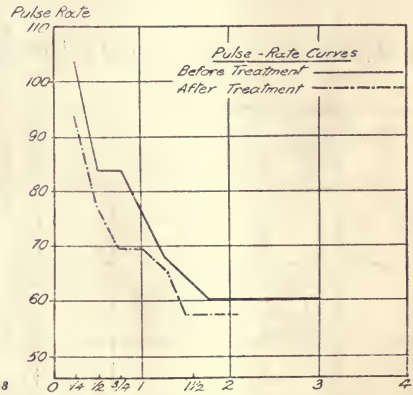
Condition when examined on October 11th, 1917.

The patient is rather fat, but on the whole a very healthy-looking man. His tongue is clean, teeth fairly good; his palate is rather injected. Nothing abnormal is found on examination of the chest, abdomen or nervous system. The urine is normal. His pulse-rate is 66; the artery is not thickened, and the pulse tension and volume are normal.

TABLE 16A.—Case 2. T. J. Pulse-rate after Exercise.

Before 1st treatment, October 11th, 1917.		*After 1st treatment, October 17th, 1917.*	
Time.	Rate per minute.	Time.	Rate per minute
Before exercise ...	66	Before exercise ...	57
1st ¼ minute ...	104	1st ¼ minute ...	84
2nd ,, ...	84	2nd ,, ...	68
3rd ,, ...	84	3rd ,, ...	**60**
4th ,, ...	76	4th ,, ...	60
5th ,, ...	**68**	5th ,, ...	56
6th ,, ...	64	6th ,, ...	48
7th ,, ...	60	7th ,, ...	48
8th ,, ...	60	8th ,, ...	48

TABLE 16B.—Case 2. T. J. The lower curve is calculated from a base line of 57.[1]



[1] In expressing these figures diagrammatically the data before and after treatment are referred to the same base line. The base line for pulse rates before treatment is 66. That, however, for the figures after treatment would be 57, but in order to bring it up to a base line of 66, 9 has been added to each pulse rate, thus 84 after treatment in Table 16A becomes 93 in Table 16B, 68 becomes 75 and so on. A better way would probably be to express all pulse rates at percentages of the resting rate.

TABLE 17A.—Case 2. T. J.

Date.	Time.	Red Cells.	Hb.
1917.		Million per cu. mm.	per cent.
October 11th ...	10 p.m.	7.87	110.5
	11.30 p.m. (entered chamber)		
„ 12th ...	10 a.m.	7.88	112
	8 p.m.	7.79	111
„ 13th ...	10 a.m.	7.45	108
	8.30 p.m.	6.95	107.5
„ 14th ...	10 a.m.	6.95	106.5
	9 p.m.	6.65	107.5
„ 15th ...	12 noon	7.10	109
	11 p.m.	6.96	108
„ 16th ...	12 noon	6.80	108
	9.30 p.m.	6.71	107
„ 17th ...	10.30 a.m. (left chamber)		
	12.30 p.m.	6.42	106

TABLE 17B.—Case 2. T. J. Blood counts and hæmoglobin values.

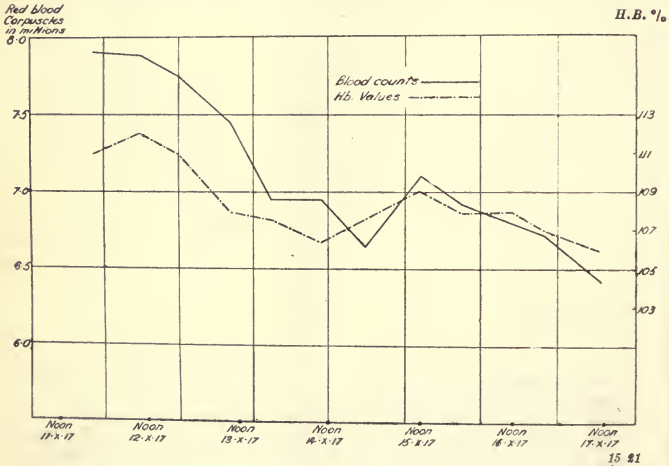
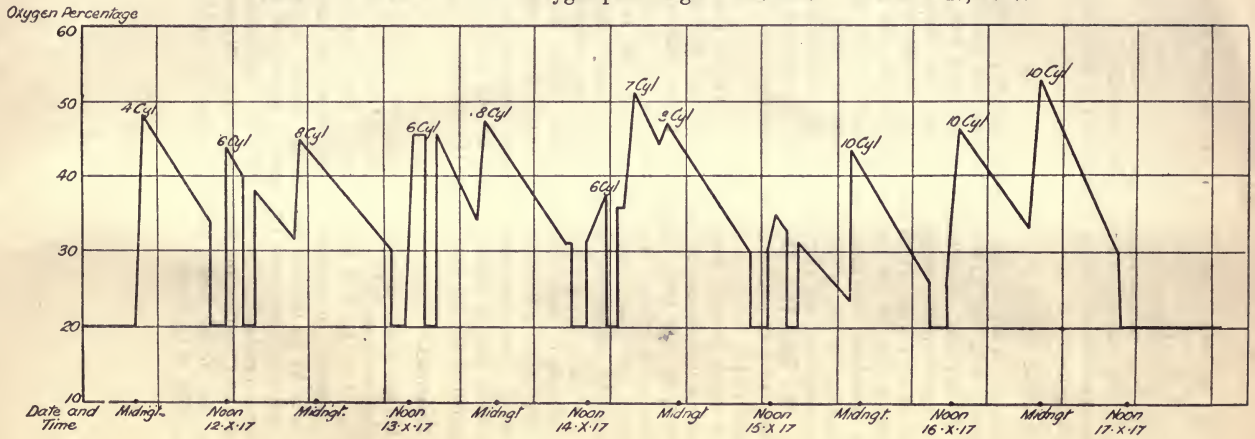


TABLE 18.—Cases 2 and 3. Oxygen percentage in chamber. October 11-17, 1917.



Walking up four flights of stairs in 1 minute 20 seconds caused much dyspnœa, but not a very marked rise of pulse-rate ; after this exercise the pulse returned to its original rate after 1¼ minutes. (See Table 16.) In a normal subject the pulse returned to its original rate within half a minute after the same exercise.

Blood examination showed 7.9 million red cells, and 110–111 per cent. hæmoglobin.

First Treatment.

He was put in the oxygen chamber at 11.30 p.m. on October 11th, and remained in it until 10.30 a.m. October 17th, except when he went out to take exercise. (See Table 18.) He slept well, and was quite free from any dyspnœa, except on October 14th when he had a very slight attack at 7 p.m., which lasted about 10 minutes.

He stated that he felt very much better for the treatment, and that his breathing was much easier when he was walking. After the treatment he was given the test exercise again ; the dyspnœa was very much less, and the pulse returned to its original rate after a minute. (See Table 16.) The polycythæmia was diminished, the red cells falling to 6.42 million ; the hæmoglobin fell to 106 per cent. (See Table 17.)

Since being treated from October 11th to October 17th his improvement in response to exercise had been maintained ; he had also been quite free from dyspnœa at night. About the middle of November he developed weakness of the left arm and leg ; on examination there was some weakness of the left arm and leg with increase of the reflexes and an extensor plantar reflex on this side ; the mode of onset was gradual, thus suggesting a cerebral thrombosis ; the Wassermann reaction was negative. After the test exercise his pulse returned to its original rate within half a minute, as it had done directly after treatment. The air expired during 5 minutes after exercise was 61 litres (normal 49 litres). His red cell count was 7.02 million and his hæmoglobin 112 per cent.

Second Treatment.

He was put in the oxygen chamber again at 7 p.m., December 15th, and remained there with intervals for exercise until 9.15 a.m., December 21st. He said he felt better, but there was no evidence that his response to exercise had improved, for his pulse returned more slowly to its original rate in one minute as against ½ minute before treatment (see Table 19), and the amount of expired air was 60.30 litres, practically the same as before treatment. His red cell count fell to 5.77 million and his hæmoglobin to 109 per cent. Possibly the fact that he felt better may have been due to this alteration in the condition of his blood.

TABLE 19.—Case 2. T. J. Pulse-rate after exercise.

Before 2nd treatment, December 15th, '17.		*After 2nd treatment, December 21st, '17.*	
Time.	Rate per minute.	Time.	Rate per minute.
Before exercise ...	74	Before exercise ...	73
1st ¼ minute ...	84	1st ¼ minute ...	100
2nd ,, ...	68	2nd ,, ...	88
3rd ,, ...	**64**	3rd ,, ...	84
4th ,, ...	56	4th ,, ...	80
5th ,, ...	64	5th ,, ...	**76**
6th ,, ...	60	6th ,, ...	68
7th ,, ...	64	7th ,, ...	68
8th ,, ...	60	8th ,, ...	68
9th ,, ...	60	9th ,, ...	72
10th ,, ...	64	10th ,, ...	72
11th ,, ...	60	11th ,, ...	68
12th ,, ...	60	12th ,, ...	68
13th ,, ...	60	4th minute ...	68
14th ,, ...	64	5th ,, ...	70
15th ,, ...	60	6th ,, ...	68
16th ,, ...	68	7th ,, ...	70
5th minute ...	64	8th ,, ...	74
6th ,, ...	64	9th ,, ...	72
		10th ,, ...	72

TABLE 20.—Case 2. T. J. (Second treatment, December 15th–21st, 1917.)

Date.	Time.	Red Cells.	Hæmoglobin.
1917.			
December 15th ...	3.30 p.m.	7.04	112
	7.0 p.m.	7.005	112
,, 16th ...	4.0 p.m.	6.58	113
,, 17th ...	10.0 a.m.	7.13	111
	3.0 p.m.	5.86	110
,, 18th ...	10,30 a.m.	6.40	110
	3.30 p.m.	5.97	110
,, 19th ...	10.30 a.m.	6.51	110
	3.45 p.m.	5.65	109
,, 20th ...	9.30 p.m.	5.72	109
,, 21st ...	9.30 a.m.	5.77	109

CASE 3.—*A. Age* 31. *Poisoning by Chloropicrin.*

History previous to being "gassed."

The patient used to do very heavy work in a colliery, and was always able to do it without any difficulty. He enlisted in March 1915, and was invalided out of the army in April 1916 for a wound of the foot. Since that time he has done heavy work in a gas factory. He has always been a healthy man.

History of being "gassed."

Since he has worked in the munition factory he has frequently been exposed to small amounts of gas. About the middle of October 1916 he states he inhaled a large quantity and had to remain in bed for 3–4 days. The immediate symptoms following this were headache, pain in the chest and abdomen, vomiting, dyspnœa, cough and lachrymation; he was not unconscious.

Symptoms subsequent to being "gassed."

1. Pain over the left costal margin; this comes on at any time of the day, and is not affected by exercise or by taking food.

TABLE 21A.—Case 3. A. Pulse-rate after Exercise.

Before treatment, October 11th, 1917.		*After treatment, October 17th, 1917.*	
Time.	Rate per minute.	Time.	Rate per minute.
Before exercise ...	88	Before exercise ...	80
1st ¼ minute ...	164	1st ¼ minute ...	152
2nd ,, ...	152	2nd ,, ...	140
3rd ,, ...	132	3rd ,, ...	120
4th ,, ...	136	4th ,, ...	120
5th ,, ...	136	5th ,, ...	96
6th ,, ...	128	6th ,, ...	100
7th ,, ...	120	7th ,, ...	100
8th ,, ...	120	8th ,, ...	104
3rd minute ...	112	3rd minute ...	94
4th ,, ...	112	4th ,, ...	91
5th ,, ...	106	5th ,, ...	**86**
6th ,, ...	103	6th ,, ...	86
7th ,, ...	102	7th ,, ...	84
8th ,, ...	100		
9th ,, ...	100		
10th ,, ...	99		
12th ,, ...	97		
14th ,, ...	96		
15th ,, ...	**94**		

TABLE 21B. Case 3. A.

The lower curve is calculated from a base line of 57.

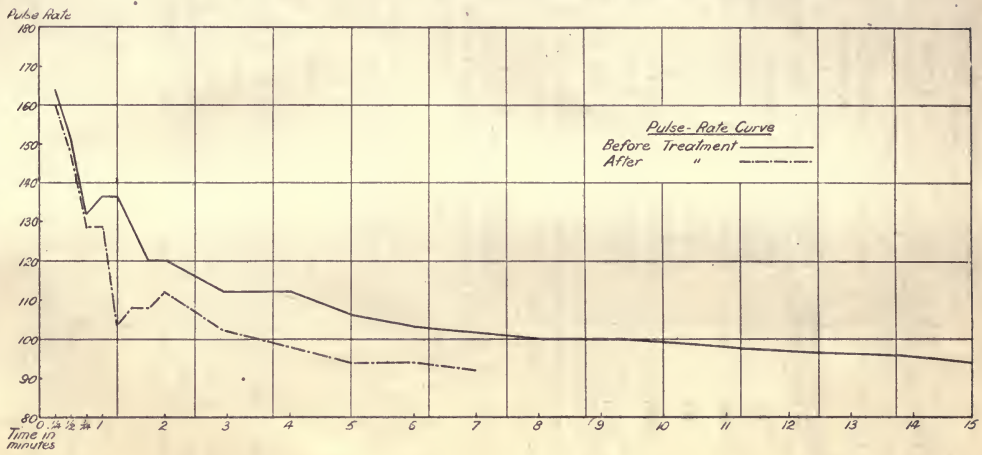
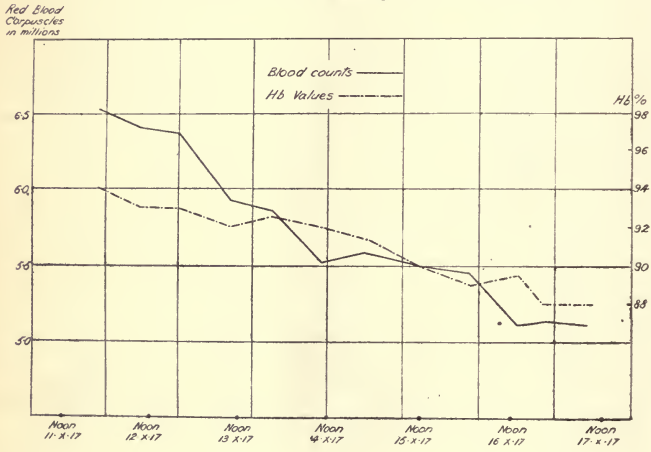


TABLE 22A.—Case 3. A.

Date.	Time.	Red Cells.	Hb.
1917.		Millions per cu. mm.	per cent.
October 11th ...	10 p.m.	6.52	94
„ 12th ...	10 a.m.	6.40	93
	8 p.m.	6.36	93
„ 13th ...	10 a.m.	5.92	92
	8.30 p.m.	5.85	92.5
„ 14th ...	10 a.m.	5.52	92
	9 p.m.	5.58	91.5
„ 15th ...	12 noon	5.50	90
	11 p.m.	5.40	89
„ 16th ...	12 noon	5.12	89.5
	9.30 p.m.	5.13	88
„ 17th ...	12.30 p.m.	5.07	88
November 29th ...	—	5.54	90

TABLE 22B.—Case 3. A.

Blood Counts and Hæmoglobin Values.



2. Dyspnœa and giddiness on exertion; this prevents him doing heavy work for any long period.

3. Dyspnœa at night; these attacks are of the usual kind; they are associated with a feeling of suffocation and tightness in the throat; they last about half-an-hour, and occur about once a week. He often sweats during an attack.

His digestion is good. He occasionally gets headaches.

Condition when examined on October 11th, 1917.

The patient is a thin, but healthy-looking man. His teeth are fairly good, tongue clean. Nothing abnormal is found on examination of the chest, abdomen or nervous system. The urine contains no albumen. The radial artery is not thickened, and the pulse is normal in volume and tension.

After walking up 10 flights of stairs in 2 minutes 45 seconds he was very dyspnœic, and the pulse only returned to its original rate after 16 minutes. (See Tables 21A and 21B.)

Blood examination showed 6.53 red cells, and 94 per cent. hæmoglobin. (See Table 22A.)

Treatment.

He was put in the oxygen chamber at 11.30 p.m. on October 11th, and remained in it until 10.30 a.m., October 17th, except when he went out for exercise. (See Table 18.) He was completely free from attacks of dyspnœa at night. His capacity to undertake exertion was greatly increased; after treatment the test exercise caused much less dyspnœa, and his pulse returned to its original rate within six minutes. (See Tables 21A and 21B.)

His red cell count fell to 5.13 millions, and his hæmoglobin to 88 per cent. (See Tables 22A and 22B.)

He fully appreciated his improvement, and is looking for regular work.

He was seen again on November 29th, and stated that he felt quite well. His red cell count was 5.54 millions with a hæmoglobin of 90 per cent.

CASE 4. *Sapper C. Age* 31.

This patient has been under the case of Lieut.-Colonel Drysdale (at St. Bartholomew's Hospital), who kindly furnished the following notes about him:—"Gassed, July 29th. Mustard burn on the buttock. First symptoms: Choking, vomiting, partial loss of voice. Later: Conjunctivitis, headache, dyspnœa, pains in the stomach. Heart 4¾ inches from the mid-line in the 5th space. Red cells, 7 million."

Previous History.

He was an electrician before joining the army. Except for occasional coughs and colds in the head, he has always been a very healthy man; he used to play football, and ran in races, and always had a very good "wind."

Symptoms subsequent to being Gassed.

1. Dyspnœa and precordial pain on slight exertion.

2. Attacks of dyspnœa at night. These attacks occur once or twice a week, and last 3–4 hours. They are accompanied by headache and a feeling of suffocation.

Condition when examined on October 21st.

The patient is a healthy-looking man. The heart's apex beat is just within the nipple line; the left border (by percussion) is 4¾ inches

from the mid-line. Nothing abnormal was found in the lungs, abdomen or nervous sytem; the urine was free from albumen. After a walk up 3 flights of stairs in 1 minute 5 seconds he was very short of breath, and his pulse returned to its original rate in 5 minutes. (See Tables 23A and 23B.) His red cell count was 6.5 million, and hæmoglobin 100 per cent. (See Tables 24A and 24B.)

TABLE 23A.—Case 4. Sapper C. Pulse-Rates after Exercise.

Before 1st treatment, October 21st, 1917.		*After 1st treatment, October 26th, 1917.*	
Time.	Rate per Minute.	Time.	Rate per Minute.
Normal	104	Normal	88
1st ¼-minute	140	1st ¼-minute	124
2nd „	124	2nd „	108
3rd „	124	3rd „	96
4th „	120	4th „	**92**
5th „	116	5th „	88
6th „	120	6th „	92
7th „	112	7th „	88
8th „	116		
9th „	118		
4th minute	112		
5th „	**108**		

Before 2nd treatment, October 31st, 1917.		*After 2nd treatment, November 3rd, 1917.*	
Time.	Rate per Minute.	Time.	Rate per Minute.
Normal	110	Normal	80
1st ¼-minute	140	1st ¼-minute	124
2nd „	128	2nd „	**84**
3rd „	120	3rd „	84
4th „	**116**	4th „	80
5th „	112	5th „	76
6th „	112		
7th & 8th ¼-minutes ...	112		

TABLE 23B.—Case 4. Sapper C.

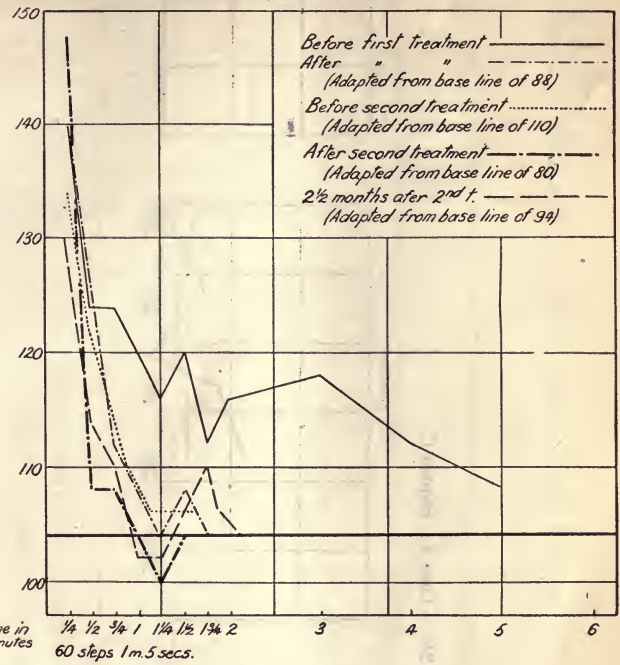


TABLE 24A.—Case 4. Sapper C.

	Date.	Time.	Red Cells.	Hb.
			Million per cu. mm.	per cent.
	1917.			
	October 21st ...	6 p.m.	6.5	100
	,, 22nd ...	12.30 p.m.	6.45	103
		8.30 p.m.	—	102
	,, 23rd ...	12.30 p.m.	5.87	101
In		8.30 p.m.	5.80	100.5
Oxygen	,, 24th ...	12.15 p.m.	6.07	100
		8.30 p.m.	5.85	98
	,, 25th ...	12.30 p.m.	5.76	96
		8.30 p.m.	5.47	95
	,, 26th ...	10 a.m.	5.00	94
		5.30 p.m.	5.24	94
	,, 31st ...	2.30 p.m.	5.68	95.5
In	November 1st ...	3.15 p.m.	5.60	93.5
Oxygen	,, 2nd ...	11 a.m.	5.40	93.5
		8 p.m.	4.80	93
	,, 3rd ...	3 p.m.	5.30	93
	,, 4th ...	3 p.m.	5.00	94
	,, 9th ...	2 p.m.	5.17	93
	1918.			
	January 23rd ...	—	6.16	98

TABLE 24B.—Case 4. Sapper C.

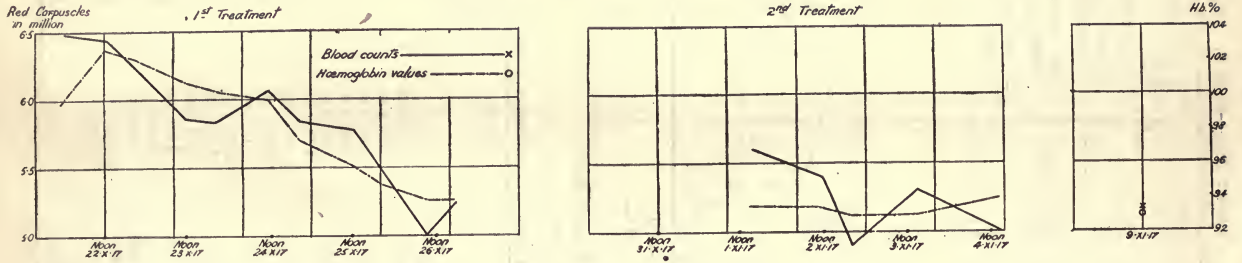
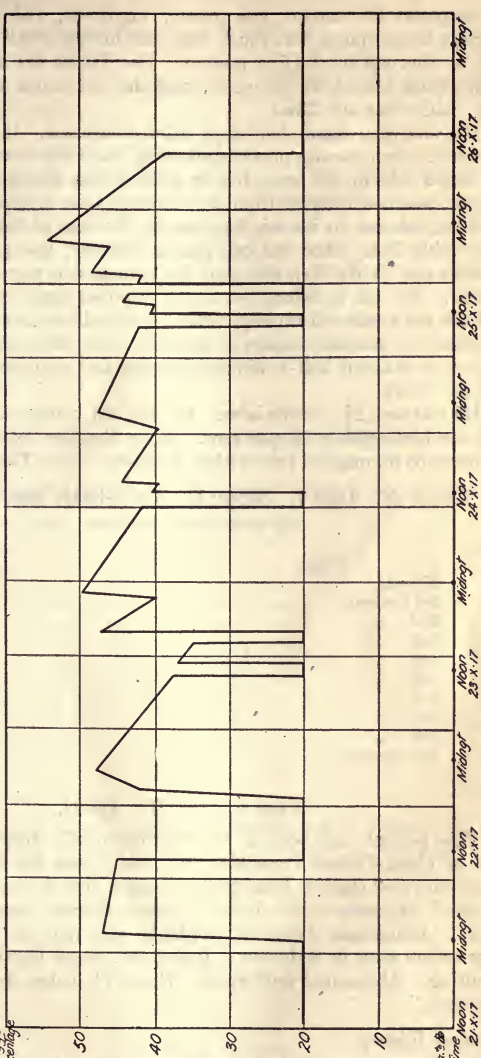


TABLE 25.—Cases 4, 5 and 6.

Oxygen Percentage in Chamber, October 21–26, 1917.



Treatment.

He was put into the chamber on October 21st at 10 p.m., and remained there, except during intervals for exercise, until 10 a.m., October 26th. (See Table 25.) He felt much better after treatment;

his response to exertion was greatly improved, and after the test exercise his dyspnœa was much less, and his pulse fell to its original rate at the end of the first minute. (See Tables 23A and 23B.) His hæmoglobin fell to 94 per cent., and the red count to 5.4 million. (See Tables 24A and 23B.)

He was seen again five days after treatment. He had had an attack of dyspnœa the previous evening, but only a very slight one. He had a cold in the head, but in spite of this the result of the test exercise was not different from that directly after treatment, the pulse returning almost to its original rate at the end of the first minute. (See Table 23A.) The red cell count, however, had gone up to 5.6 millions (see Table 24A), although the hæmoglobin percentage had not altered. He was therefore put in the chamber again (see Table 24B), and the red count fell rapidly, reaching 4.8 million in two days. His response to exercise improved further, the pulse returning to its original rate about half-a-minute after the test exercise. (See Tables 23A and 23B.)

He was seen 2½ months later. His red cell count was 6.16 million, and his hæmoglobin 98 per cent. After the test exercise his pulse returned to its original rate within ¾ minute. (See Table 26.)

TABLE 26.—Case 4. Sapper C. Pulse-Rates after Exercise.

2½ months after treatment.

Time.	Rate per Minute.
Normal	94
1st ¼-minute	120
2nd „	104
3rd „	**100**
4th „	92
5th „	88
6th „	100
7th „	100
8th „	96
3rd minute	94

CASE 5.—*Pte. D. Age* 23.

This patient had been at St. Bartholomew's Hospital under the care of Lieut.-Colonel Drysdale, who kindly sent the following notes about him :—"Gassed, June 21st, by British trench mortar gas. Five minutes' exposure; box helmet worn. Helmet removed on 'All clear.' Immediate dyspnœa, headache and nausea. Half-an-hour later severe pain in abdomen. June 23rd, cough began; June 24th, vomiting. Abdominal tenderness. Heart 4½ inches from mid-line in 5th space."

Previous History.

The patient was a bicycle maker before joining the army, and was accustomed to fairly heavy work. He used to play football, and was never troubled with shortness of breath. He stated that occasionally he had "fainting attacks," but never consulted a doctor. (These attacks do not seem to have been epileptic.) Apart from this he was always a healthy man.

Present Symptoms.

1. Dyspnœa and abdominal pain on exertion.
2. Occasional headache.

He sleeps well, and does not get any attacks of dyspnœa at night. His digestion is good.

Condition when examined on October 21st.

The patient was a healthy looking man. The heart's apex was ½ inch internal to the nipple line; the left border (by percussion) was 4½ inches from the mid-line. Nothing abnormal was found in the lungs or nervous system. There was slight tenderness in the epigastrium; otherwise the abdomen was normal. The urine was free from albumen. After a walk up 5 flights of stairs in 1 minute 5 seconds he was very short of breath and his pulse returned to its original rate after 1¾ minutes. (See Table 27.) His red cell count was 6.25 million, and his hæmoglobin was 104.5 per cent. (See Tables 28A and 28B.)

TABLE 27A.—Case 5. Pte. D. Pulse-Rates after Exercise.

Before 1st treatment, October 21st, 1917.		*After 1st treatment, October 26th, 1917.*	
Time.	Rate per Minute.	Time.	Rate per Minute.
N.	72	N.	82
1st ¼-minute	144	1st ¼-minute	124
2nd ,, ...	116	2nd ,, ...	100
3rd ,, ...	100	3rd ,, ...	**84**
4th ,, ...	80	4th ,, ...	80
5th ,, ...	80	5th ,, ...	76
6th ,, ...	80	6th ,, ...	76
7th ,, ...	**72**		

Before 2nd treatment, October 31st, 1917.		*After 2nd treatment, November 4th, 1917.*	
Time.	Rate per Minute.	Time.	Rate per Minute.
N.	84	N.	88
1st ¼-minute	124	1st ¼-minute	112
2nd ,, ...	100	2nd ,, ...	96
3rd ,, ...	**84**	3rd ,, ...	**88**
4th ,, ...	80	4th ,, ...	88
5th ,, ...	76	5th ,, ...	92
		6th ,, ...	88

TABLE 28A.—Case 5. Pte. D.

	Date.	Time.	Red Cells.	Hb.
	1917.		Million per cu. mm.	per cent.
In Oxygen	October 21st ...	6 p.m.	6.25	104.5
	,, 22nd ...	12.30 p.m.	6.15	103
		8.30 p.m.	—	—
	,, 23rd ...	12.30 p.m.	6.40	104
		8.30 p.m.	6.42	104
	,, 24th ...	12.15 p.m.	6.15	101
		8.30 p.m.	6.53	100
	,, 25th ...	12.30 p.m.	5.30	—
		8.30 p.m.	5.20	97
	,, 26th ...	10 a.m.	5.40	97
		5.30 p.m.	5.10	96
	,, 31st ...	2.30 p.m.	6.02	103.5
In Oxygen	November 1st ...	3.15 p.m.	6.08	97 (?)
	,, 2nd ...	11 a.m.	5.74	100
		8 p.m.	5.39	99
	,, 3rd ...	3 p.m.	5.20	98
	,, 4th ...	3 p.m.	5.03	97
	,, 9th ...	2 p.m.	5.19	100
	1918.			
	January 23rd ...	—	5.21	102

TABLE 27B.—Case 5. Pte. D.

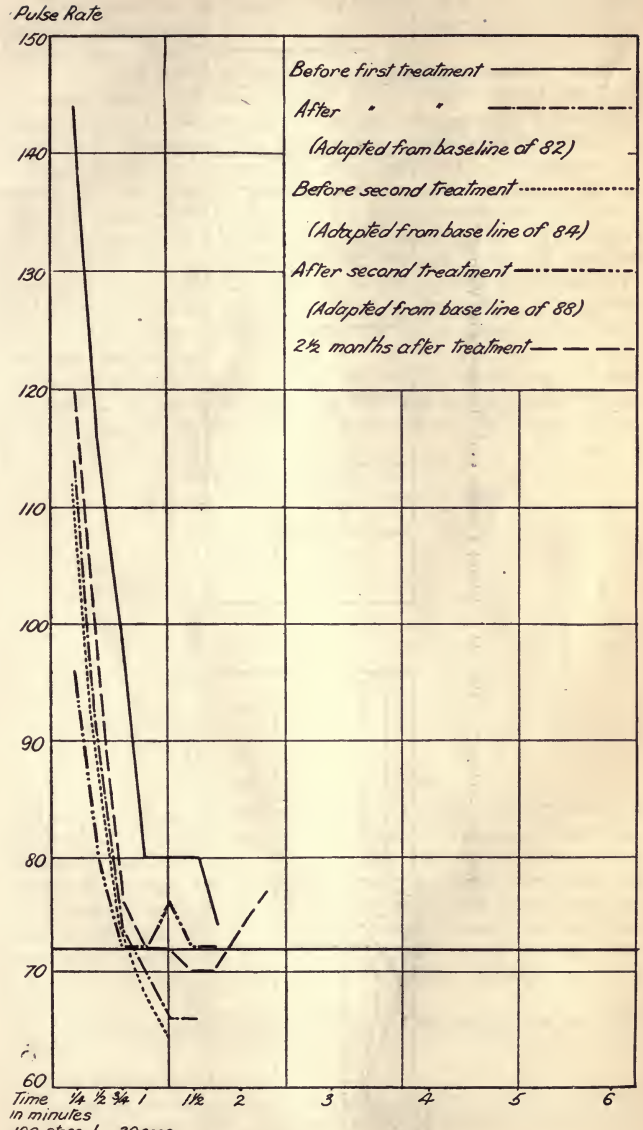
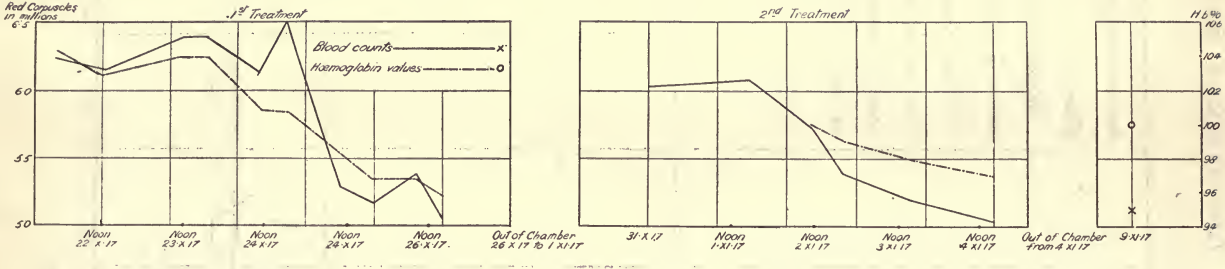


Table 28B.—Case 5. Pte. D. Blood Counts and Hæmoglobin Values.



Treatment.

He was put into the chamber on October 21st, at 10 p.m., and remained there, except during intervals for exercise, until 10 a.m., October 26th. (See Tables 10 and 25.)

He felt much better after treatment, and his response to exercise was much improved; after the test exercise his dyspnœa was less, and his pulse fell to its original rate within three-quarters of a minute. His red cells fell to 5.1 million, and his hæmoglobin to 96 per cent.

He was seen again three days after treatment. The response to exercise was not quite so good as directly after treatment, but his pulse still returned to its original rate after the exercise within one minute. The red cell count however, had risen to 6.08, and the hæmoglobin to 103.5 per cent. He was therefore put into the chamber again from 6 p.m., November 1st, until 3 p.m., November 4th (see Table 28B), and the red count fell to 5.03 in three days. (See Tables 28A and 28B.) After exercise his pulse returned to normal within three-quarters of a minute.

He was seen 2½ months later. His red cell count was 5.21 and hæmoglobin 102 per cent. After the test exercise, his pulse returned to its original rate within three-quarters of a minute. (See Tables 28B and 29.)

TABLE 29.—Case 5. Pte. D.

2½ months after treatment, January 23rd, 1918.

Time.	Rate per Minute.
N.	72
1st ¼-minute	120
2nd „	96
3rd „	**76**
4th „	72
5th „	72
6th „	68
7th „	68
8th „	72
3rd minute	76

CASE 6.—*Pte. A. Age* 20.

This patient had been at St. Bartholomew's Hospital under the care of Lieut.-Col. Drysdale, who kindly sent the following notes about him. "Gassed, June 30th, 1917. Phosgene (?). Helmet not in use. First symptoms: cough and choking, increasing dyspnœa, increasing pain in the chest, no lachrymation. Onset 5 minutes after exposure; vomiting one hour later, continuing for 8 days. Heart's left border by percussion, 5 inches from mid-line in 5th space; some cyanosis. Red cell count 6.37 million; leucocyte count 7600; hæmoglobin 93 per cent.

"Still suffers from dyspnœa, headache and palpitation on slight exertion."

Previous History.

The patient was in the boot and shoe trade before joining the army; the work was quite light. He used to play football, and this did not cause him any abnormal dyspnœa.

Present Symptoms.

1. Dyspnœa, headache and precordial pain on exertion; he states that he cannot walk more than a mile without considerable discomfort.

2. Dyspnœa at night. This comes on in attacks, which are associated with headache and a feeling of suffocation. The attacks occur every other night, and last a quarter to half-an-hour.

His digestion is good.

Condition when examined on October 21*st.*

The patient was a thin, rather weakly-looking man. The left border of the heart by percussion was 5 inches from the mid-line in the fifth space. Nothing abnormal was found in the lungs, abdomen or nervous system. The urine was free from albumen. After a walk up 2 flights of stairs in 41 seconds he was very short of breath, and the pulse returned to its original rate within a minute. (See Tables 30A and 30B.) His red cell count was 6 million, and his hæmoglobin 93 per cent. (See Tables 31A and 31B.)

TABLE 30A.—Case 6. Pte. A. Pulse-rates after Exercise.

Before treatment, October 21st, 1917.		After treatment, October 26th, 1917.		After treatment, October 31st, 1917.	
Time.	Rate per Minute.	Time.	Rate per Minute.	Time.	Rate per Minute.
N.	94	N.	102	N.	102
1st ¼ minute	132	1st ¼-minute	136	1st ¼ minute	132
2nd ,, ...	108	2nd ,,	**108**	2nd ,,	**108**
3rd ,, ...	104	3rd ,,	108	3rd ,,	104
4th ,, ...	**96**	4th ,,	104	4th ,,	108
5th ,, ...	96	5th ,,	104	5th ,,	104

TABLE 30B.—Case 6. Pte. A.

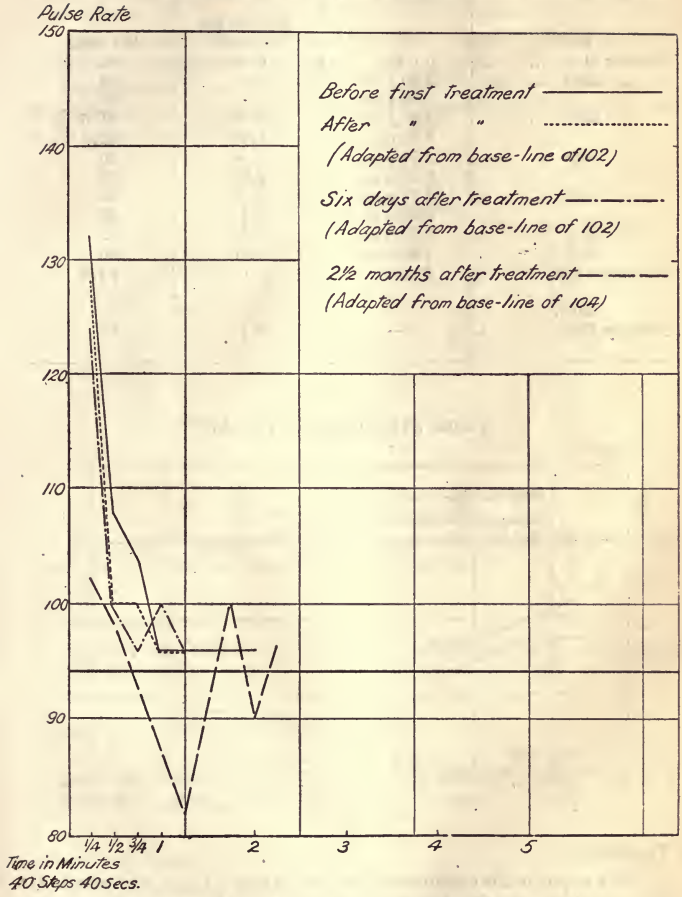
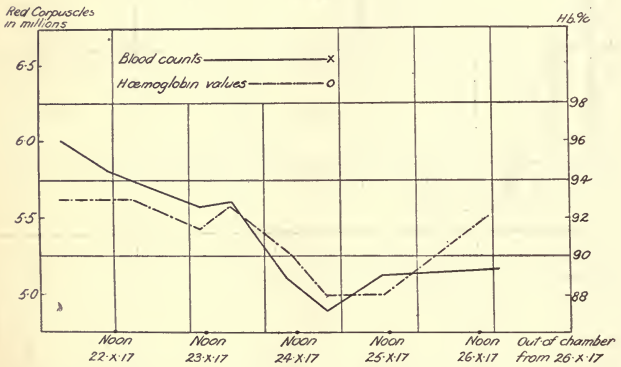


TABLE 31A.—Case 6. Pte. A.

Date.	Time.	Red Cells.	Hb.
		Millions per cu. mm.	Per cent.
1917.			
October 21st	6 p.m.	6.0	93
„ 22nd	12.30 p.m.	5.7	93
	8.30 p.m.	—	93
„ 23rd	12.30 p.m.	5.58	91.5
	8.30 p.m.	5.60	92.5
„ 24th	12.15 p.m.	5.08	90
	8.30 p.m.	4.91	88
„ 25th	12.30 p.m.	5.17	88
	8.30 p.m.	5.15	92
„ 26th	2.30 p.m.	5.13	92
„ 31st	2.30 p.m.	5.40	100
November 9th	2 p.m.	5.0	93.5
1918.			
January 23rd	—	5.7	98

TABLE 31B.—Case 6. Pte. A.



Treatment.

He was put in the chamber on October 21st at 10 p.m., and remained there until 10 a.m., October 25th. He felt much better after the treatment; while in the oxygen he was completely free from dyspnœa at night, and his headaches almost disappeared. His dyspnœa on exertion was much less, and after the test exercise his pulse returned to its original rate within half a minute. (See Table 30A.)

His red cell count had fallen to 5.87, and his hæmoglobin to 88 per cent. (See Tables 31A and 31B.)

The table below shows the hæmoglobin percentage and red cell counts on three subsequent occasions.

Date.	Red Cell Count.	Hæmoglobin.
October 26th	5.15 million	92 per cent.
October 31st	5.4 million	100 per cent.
November 9th	5.01 million	93.5 per cent.

After the test exercise on October 31st, his pulse returned to its original rate within half a minute.

He was seen 2½ months later. His red cell count was 5.7 million and hæmoglobin 98 per cent. After the test exercise his pulse returned to its original rate within ½ minute.

TABLE 32.—Case 6. Pte. A.

2½ months after treatment.

Time.	Rate per Minute.
N.	... 104
1st ¼-minute	... 112
2nd ,, ...	... **108**
3rd ,, ...	... 100
4th ,, ...	... 92
5th ,, ...	... 100
6th ,, ...	... 104
7th ,, ...	... 112
8th ,, ...	... 100
3rd minute	... 106

CASE 7.—*Sgt. S. Age* 36.

This patient was gassed with chlorine on April 24th, 1915, the first occasion on which gas was used by the Germans.

History previous to being gassed.

He had done heavy work all his life, and was a good athlete, having rowed and swum in races. He had had no serious illness.

Symptoms immediately after being gassed.

These were cough, dyspnœa and pain across the chest; he did not vomit. He expected to recover in a day or two, but gradually got worse, and went to hospital on May 2nd.

Present symptoms.

1. Dyspnœa on exertion.
2. Headache, especially on waking up in the morning.
3. Constipation. His bowels are only open three times a week, although he takes paraffin, and often pills at night and salts in the morning.

His digestion is good. He used to get attacks at night, during which he felt faint, and had a sensation of tightness in the chest, but these attacks have now ceased.

Condition when examined on October 30th.

The patient is a spare, but very healthy looking man. Nothing abnormal is found in the chest, abdomen or nervous system; the urine is free from albumen. A walk up five flights of stairs in 1 minute 40 seconds caused much dyspnœa, and the pulse did not return to its original rate for ten minutes. (See Tables 33A and 33B.) His red cell count was 5.93 million and his hæmoglobin 104 per cent. (See Tables 34A and 34B.)

TABLE 33A.—Case 7. Sgt. S. Pulse-Rate after Exercise.

Before treatment, October 30th, 1917.		*After treatment, November 4th, 1917.*	
Time.	Rate per Minute.	Time.	Rate per Minute.
N.	62	N.	62
1st ¼-minute	—	1st ¼-minute	100
2nd ,, ...	120	2nd ,, ...	80
3rd ,, ...	116	3rd ,, ...	76
4th ,, ...	104	4th ,, ...	64
5th ,, ...	100	5th ,, ...	68
6th ,, ...	92	6th ,, ...	68
7th ,, ...	96	7th ,, ...	64
8th ,, ...	92	8th ,, ...	60
3rd minute	84		
4th ,, ...	84		
5th ,, ...	76		
6th ,, ...	72		
7th ,, ...	70		
8th ,, ...	69		
9th ,, ...	69		
10th ,, ...	68		
11th ,, ...	68		
12th ,, ...	68		

TABLE 33B.—Case 7. Sgt. S.

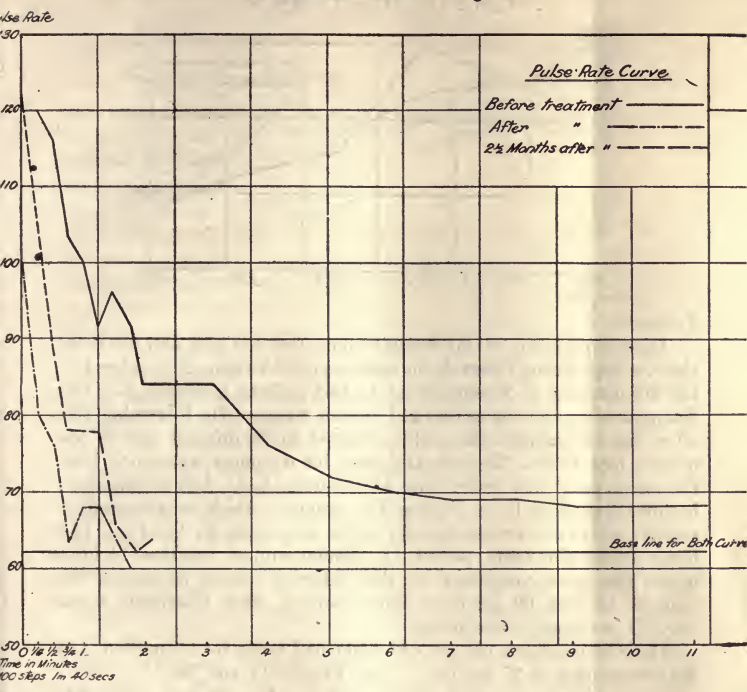
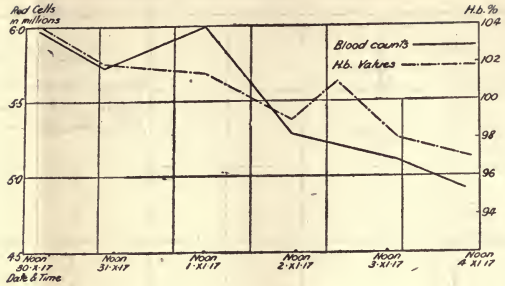


TABLE 34A.—Case 7. Sgt. S.

Date.	Time.	Red Cells.	Hb.
		Millions per cu. mm.	per cent.
1917.			
October 30th	6 p.m.	5.93	104
,, 31st	10 a.m.	5.72	102
	6 p.m.	6.0	101.5
November 1st	10 a.m.	5.3	99
,, 2nd	10 p.m.	5.2	101
,, 3rd	3 p.m.	5.1	98
,, 4th	10.30 a.m.	4.9	97
1918.			
January 23rd	—	5.22	99

TABLE 34B.—Case 7. Sgt. S.



Treatment.

He was put in the chamber at 6.30 p.m., October 31st, and remained there, except during intervals for exercise, until 10 a.m., November 4th. On the morning of November 1st he had a slight headache, but this disappeared in an hour or two and did not return. On November 4th, after the test exercise, his pulse returned to its original rate in one minute (see Tables 33A and 33B), and his dyspnœa was much less; the latter point was tested with the Douglas bag; before treatment he breathed 21.3 litres during the minute which commenced 30 seconds after this exercise ceased; after treatment he breathed 17.5 litres during the same period; a normal subject breathes 14 litres under the same conditions, so that whereas before treatment S.'s expired air was 69 per cent. above normal, after treatment it was only 35 per cent. above normal.

On November 4th his red cell count had fallen to 4.9 million, and his hæmoglobin to 97 per cent. (See Tables 34A and 34B.)

He was seen again on January 23rd. His red cell count was 5.22 million and hæmoglobin 99 per cent. After the test exercise his pulse returned to its original rate within 1¾ minutes.

TABLE 35.—Case 7. Sgt. S.

Pulse-Rate after Exercise, 2½ months, date January 23rd, 1918.

Time.	Rate per Minute.
N.	68
1st ¼-minute	128
2nd ,, ...	112
3rd ,, ...	96
4th ,, ...	84
5th ,, ...	84
6th ,, ...	84
7th ,, ...	**72**
8th ,, ...	68
3rd minute	70

CASE 8.—*A. Age* 59.

History previous to being gassed.

The patient had never had any serious illness, and stated that he had always been a very healthy man. He had been accustomed

to heavy work as an engineer, and had always been able to do it without dyspnœa or pain in the chest.

Symptoms immediately after being gassed with Chlorine, 50°/₀ + *Phosgene*, 50₀/°.

He was not unconscious, but started to cough violently and became very short of breath; vomiting started a week later, but soon stopped. He stated that within a few hours his "whole body swelled." He also had severe precordial pain.

Present Symptoms.

1. Dyspnœa on exertion.

2. Precordial pain. This is brought on by exercise, but also occurs at night, when it comes on in attacks and is associated with a feeling of constriction in the chest; he has these attacks nearly every night, and they last one to two hours. He was seen during one of these attacks; he complained of feeling faint and of pain over the heart; he was sweating slightly, and there was hyperæsthesia over the precordium and down the left arm; there was no alteration in the pulse rate or tension, but the normal rhythm was interrupted by numerous extra systoles. The attack was quite different from the nocturnal dyspnœa associated with the polycythæmia following "gassing," and appeared to be identical with those met with in old people suffering from myocardial degeneration. (The symptoms and condition of the patient were not sufficiently serious for the attack to merit the description of "Angina Vera.")

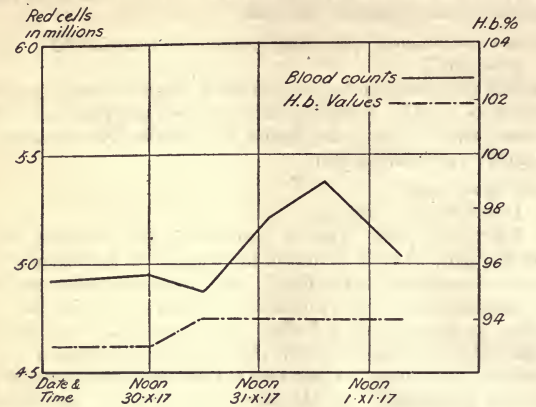
Condition when examined on October 20th.

The patient is a feeble old man. His pulse is intermittent, the result of occasional extrasystoles; the blood pressure is 114 mm. Hg., and the radial artery is not abnormally thick for a man of his age. His heart is not enlarged, and the sounds are normal. There are no signs of aneurism. Nothing abnormal is found in the lungs or abdomen. His gait is hesitating when going up and down stairs, but there are no abnormal signs in the nervous system. The urine is free from albumen. After walking 100 yards along the level he breathed 21.51 litres in two minutes, starting half-a-minute after his return; owing to the irregularity of the pulse it was not possible to obtain reliable observations on its rate. His red cell count was 4.92 million, and his hæmoglobin 93 per cent. (See Tables 36A and 36B.)

TABLE 36A.—Case 8. A. A.

Date.	Time.	Red Cells.	Hb.
1917.		Millions per cu. mm.	per cent.
October 29th	6 p.m.	4.92	93
	11.30 p.m. (entered chamber)		
„ 30th	12 noon	4.95	93
	10 p.m.	4.86	94
„ 31st	10 a.m.	5.20	94
	6 p.m.	5.37	94
November 1st	10 a.m. (left chamber)	5.03	94

TABLE 36B.—Case 8. A. A. Blood Counts and Hæmoglobin Values.



Treatment.

He was put in the chamber at 11.30 p.m. on October 29th and remained there, with intervals for exercise, until 10 a.m. on November 1st. He stated that he felt much better, and that his breathing was much easier when walking. That his dyspnœa on exertion was less after treatment was confirmed by using the Douglas bag, for after the test exercise he only breathed 17.5 litres in two minutes. He still had attacks of pain at night, but said they were much less severe. His red cell count was 5.03, and his hæmoglobin 94 per cent. (See Tables 36A and 36B.)

CASE. 9.—*Pte. O'B. Age* 22.

This patient had been under the care of Lieut.-Col. Drysdale at St. Bartholomew's Hospital.

Previous History.

He had always been a very healthy man, and went in for various games and athletics; he had never been troubled with any shortness of breath.

History of being gassed.

He was gassed on September 9th, 1917. He felt dazed at first, and about five hours later the following symptoms began to appear, conjunctivitis, laryngitis and cough; the first two disappeared after a few days, but he was kept in bed on account of "chest trouble" for three weeks. He had no burns.

Present Symptoms.

He complains of dyspnœa and precordial pain on slight exertion. Sleep is often disturbed by cough but he has no attacks of nocturnal dyspnœa.

Condition when examined, November 14th.

The patient is a healthy looking man. He has a soft basal and apical systolic murmur, which is clearly "functional," but beyond this,

nothing abnormal is found in the chest, abdomen or nervous system. His response to exercise was tested by making him walk up 3 flights of stairs in 1 minute 15 seconds; his pulse returned to its original rate in the fifth minute afterwards. (See Table 37.) He complained of precordial pain, and it was obvious that the exercise caused him distress. His red cell count was 4.8 million, and his hæmoglobin 88 per cent. (See Table 38.)

TABLE 37.—Case 9. Pte. O'B. Pulse-Rates after Exercise.

Before treatment, November 14th, 1917.		*After treatment, November 21st, 1917.*	
Time.	Rate per Minute.	Time.	Rate per Minute.
N.	80	N.	66
1st ¼-minute	112	1st ¼-minute	92
2nd ,, ...	92	2nd ,, ...	84
3rd ,, ...	88	3rd ,, ...	**68**
4th ,, ...	88	4th ,, ...	60
5th ,, ...	88	5th ,, ...	64
6th ,, ...	88	6th ,, ...	68
7th ,, ...	92	7th ,, ...	64
8th ,, ...	—		
3rd minute	92		
4th ,, ...	94		
5th ,, ...	**86**		
6th ,, ...	86		

TABLE 38.—Case 9. Pte. O.'B.

Date.	Time.	Red Cells.	Hb.
		Millions per cu. mm.	per cent.
1917.			
November 14th ...	5 p.m.	4.80	88
	10.45 p.m. (entered chamber)		
,, 15th ...	10.30 a.m.	4.94	—
	7 p.m.	5.15	88
,, 16th ...	10 a.m.	4.96	88
	9 p.m.	5.0	88
,, 17th ...	10.30 a.m.	4.95	86
	7 p.m.	4.83	87
,, 18th ...	10 a.m.	4.84	88
	7 p.m. (left chamber)	5.00	87
,, 19th ...	10 a.m.	4.9	87
,, 22nd ...	—	4.75	93
,, 24th ...	—	4.40	94
,, 26th ...	—	4.80	91
,, 28th ...	—	5.04	93
December 1st ...	—	4.81	91
1918.			
January 23rd ...	—	5.3	88

Treatment.

He was put in the oxygen chamber at 10.45 p.m., November 14th, and remained there, with intervals for exercise, until 9.30 a.m., November 19th. He felt much better after the treatment, and able to stand more exertion; the test exercise caused him no distress, and his pulse returned to its original rate within ¾ minute (see Table 37) after his return from it.

A similar result was obtained after a test on December 1st.

His red cell count and hæmoglobin percentage showed no appreciable alteration throughout the treatment and during the subsequent fortnight, and in this respect was in sharp contrast to those found in cases of polycythæmia.

He was re-examined on January 23rd. After the test exercise his pulse rate fell within ½ minute to its original rate. (See Table 39.) His red cell count was 5.3 million and hæmoglobin 88 per cent.

TABLE 39.—Case 8. Pte. O'B.

2 months after treatment, January 23rd, 1918.

Time.	Rate per minute.
N.	80
1st ¼-minute	92
2nd „	**76**
3rd „	64
4th „	68
5th „	64
6th „	64
7th „	72
8th „	68

CASE 10.—*Gnr. A. Aged* 19. *Mustard Gas.*

Previous History.

The patient had always been a very healthy man, and was accustomed to take plenty of hard exercise; his "wind" had always been good.

History of being gassed.

He was gassed on September 28th, 1917. He was not actually burnt but his skin "peeled." He had conjunctivitis for some weeks. He also had much cough and expectoration.

Present Symptoms.

He complains of dyspnœa, thumping in the chest and headache on exertion. He sleeps well, and has no dyspnœa at night.

Condition when examined on November 14th.

The patient is a sparely-built but healthy looking man. He has a soft, localised, apical murmur, systolic in time and obviously only "functional"; otherwise nothing abnormal is found in the chest, abdomen or nervous system. After walking up 4 flights of stairs in 1 minute 20 seconds, his pulse rate was still ten beats per minute above its original rate at the end of the ninth minute, and he was very short of breath. (See Table 40.)

His red cell count was 6.25 million and his hæmoglobin 101 per cent. (See Table 41.)

TABLE 40.—Case 10. Gnr. A. Pulse-Rates after Exercise.

Before treatment, November 14th, 1917.		*After treatment, November 21st, 1917.*	
Time.	Rate per Minute.	Time.	Rate per Minute.
N.	88	N.	68
1st ½-minute	144	1st ½-minute	116
2nd ,, ...	124	2nd ,, ...	84
3rd ,, ...	108	3rd ,, ...	80
4th ,, ...	96	4th ,, ...	80
2nd minute	96	5th ,, ...	68
3rd ,, ...	100	6th ,, ...	72
4th ,, ...	104	7th ,, ...	68
5th ,, ...	104	8th ,, ...	68
6th ,, ...	102		
7th ,, ...	100		
8th ,, ...	102		
9th ,, ...	98		
10th ,, ...	100		
17th ,, ...	96		
18th ,, ...	95		
22nd ,, ...	95		
23rd ,, ...	96		
24th ,, ...	96		

TABLE 41.—Case 10. Gnr. A.

Date.	Time.	Red Cells.	Hb.
		Million per cu. mm.	per cent.
1917.			
November 14th ...	5 p.m.	6.25	101
	10.45 p.m. (entered chamber)		
,, 15th ...	10.30 a.m.	6.12	101
	7 p.m.	6.00	101
,, 16th ...	10 a.m.	5.73	97
	9 p.m.	5.64	101
,, 17th ...	10.30 a.m.	5.67	100
	7 p.m.	5.95	96
,, 18th ...	10 a.m.	5.20	92
	7 p.m.	5.55	86
,, 19th ...	10 a.m.	6.00	92
	6 p.m.	5.38	94
,, 20th ...	10 a.m.	5.40	92
	7 p.m.	5.35	90
,, 21st ...	10 a.m. (left chamber)	5.26	92
,, 22nd ...	—	5.80	92
,, 24th ...	—	5.89	93
,, 26th ...	—	6.60	93
,, 28th ...	—	5.80	92
December 1st ...	—	5.70	91
1918.			
January 23rd ...	—	6.20	98

Treatment.

He was put in the oxygen chamber at 10.45, November 14th, and remained there, with intervals for exercise, until 10 a.m., November 21st.

He felt much less breathless on exertion after the treatment, and this improvement persisted for the remainder of the time (a fortnight) during which he was under observation; on November 21st, the test exercise caused no abnormal amount of dyspnœa, and his pulse afterwards returned to its original rate after one minute; a similar result was found on December 1st. (See Table 40.)

His red cell count fell more slowly than is usually the case, being 5.26 million on November 21st, with a hæmoglobin of 92 per cent. It rose again subsequently, being 5.7 million on December 1st with a hæmoglobin of 91 per cent. (See Table 41.)

He was re-examined on January 23rd. After the test exercise his pulse returned to its original rate after one minute. (See Table 42.) His red cell count was 6.2 million with a hæmoglobin of 98 per cent.

TABLE 42.—Case 10. Gnr. A.

2 months after treatment, January 23rd, 1917.

Time.	Rate per minute.
N.	78
1st ½ minute	140
2nd „	112
3rd „	100
4th „	96
5th „	**80**
6th „	80
7th „	84
8th „	80

CASE. 11.—*Cpl. H. H. Age* 22. *Mustard Gas.*

This patient had been under the care of Lieut.-Col. Drysdale at St. Bartholomew's Hospital.

Previous History.

The patient was a grocer's assistant before enlisting. He did not do very heavy work, but was a fair athlete and able to cycle 40 miles a day without any undue fatigue.

History of being gassed.

He was gassed on August 1st, 1917. He was burnt particularly on the arms, and also suffered from conjunctivitis, which was very resistent to treatment. He was kept in bed for eight weeks for "chest trouble." He stated that he became unconscious about eight hours after being gassed, and remembered nothing until he arrived in England about a fortnight later.

Present Symptoms.

He complains of pain in the chest and dyspnœa on exertion. For some weeks after being gassed he suffered from headache, but this has now passed off. He sleeps well, and has no dyspnœa at night.

Condition when examined, November 14th.

He is a healthy looking man. Nothing abnormal is found on examination of the chest, abdomen or nervous system. There is some opacity of the cornea of the left eye, and the conjunctiva is rather inflamed. There are some scars of burns on both arms.

After walking up 10 flights of stairs in 3 minutes 40 seconds, he was very short of breath, and 15 minutes after his return from the exercise his pulse was still 21 beats per minute above its original rate. (See Table 43.) His red cell count was 5.57, and his hæmoglobin 111 per cent. (See Table 44.)

TABLE 43.—Case 11. Cpl. H. H.

Before treatment, November 14th, 1917.		*After treatment, November 19th, 1917.*	
Time.	Rate per Minute.	Time.	Rate per Minute.
N.	75	N.	86
1st ¼-minute	140	1st ¼-minute	140
2nd ,, ...	120	2nd ,, ...	120
3rd ,, ...	116	3rd ,, ...	116
4th ,, ...	112	4th ,, ...	108
5th ,, ...	104	5th ,, ...	112
6th ,, ...	100	6th ,, ...	112
7th ,, ...	100	7th ,, ...	104
8th ,, ...	100	8th ,, ...	108
3rd minute	100	3rd minute	100
4th ,, ...	100	4th ,, ...	110
5th ,, ...	96	5th ,, ...	110
7th ,, ...	100	6th ,, ...	112
8th ,, ...	102	7th ,, ...	108
9th ,, ...	104	9th ,, ...	110
11th ,, ...	100	10th ,, ...	112
15th ,, ...	96	11th ,, ...	104
19th ,, ...	86	12th ,, ...	104
21st ,, ...	86	13th ,, ...	104
23rd ,, ...	90	14th ,, ...	100
27th ,, ...	86	15th ,, ...	100
35th ,, ...	86	16th ,, ...	100
39th ,, ...	84	18th ,, ...	102
50th ,, ...	80	20th ,, ...	100
		22nd ,, ...	98
		25th ,, ...	100
		27th ,, ...	100
		30th ,, ...	98
		32nd ,, ...	100
		35th ,, ...	94
		37th ,, ...	98
		40th ,, ...	92
		42nd ,, ...	96
		47th ,, ...	96

TABLE 44.—Case 11. Cpl. H. H.

Date.	Time.	Red Cells.	Hb.
		Millions per cu. mm.	per cent.
1917.			
November 14th ...	5 p.m.	5.57	111
	10.45 p.m. (entered chamber)		
„ 15th ...	10.30 a.m.	5.75	109
	7 p.m.	5.65	111
„ 16th	10 a.m.	5.33	104
	9 p.m.	5.40	—
„ 17th ...	10.30 a.m.	5.20	104
	7 p.m.	5.33	102
„ 18th ...	10 a.m.	5.20	101
	7 p.m.	4.90	97
„ 19th ...	9.30 a.m. (left chamber)	—	—
	10 a.m.	5.10	102
„ 22nd ...	—	5.50	100
„ 24th ...	—	5.50	98
„ 26th ...	—	5.50	99
„ 28th ...	—	5.40	102
December 1st ...	—	5.70	101
1918. ...			
January 23rd ...	—	5.36	102

Treatment.

He was put in the oxygen chamber at 10.45 p.m., November 14th, and remained there, with intervals for exercise, until 9.30 a.m., November 19th. He felt much less short of breath after the treatment, but at first there was not much improvement as judged by his pulse rate, the pulse still being fourteen beats above its original rate at the end of the fifteenth minute after his return. (See Table 43.) The same test, however, was applied on December 1st and December 7th, and on both occasions the pulse returned to its original rate within 1¼ minutes.

His hæmoglobin fell to 102 per cent. and his red count to 5.1 million; for the next fortnight his hæmoglobin remained fairly constant, but his red count rose again to its original figure and sometimes above it. (See Table 44.)

When seen on December 7th he was quite confident that his improved response to exercise was persisting, a statement which was born out by the reaction of his pulse mentioned above.

He was re-examined on January 23rd. His red cell count was 5.36 million with a hæmoglobin of 102 per cent. It was not possible to carry out any exercise test, as he was being kept in bed on account of a corneal ulcer, which would not heal while he was up and walking.

CASE 12.—*Lt. P. Age* 23.

History previous to being Gassed.

The patient was always a very healthy man, and used to play football and box. He did a 15-mile march in July, 1917, without any difficulty.

History of being Gassed.

He was gassed on September 11th. He thinks the gas was phosgene. The first symptoms, which came on within 10 minutes of being gassed, were vomiting, headache, pain right across the chest, cough and dyspnœa. He also had slight lachrymation for two days, and some small boils on the neck, but no actual burns.

Present Symptoms.

He complains of dyspnœa on exertion, and can only walk about 1½ miles at a stretch, and this takes him ¾ hour. He also has spasmodic attacks of dyspnœa associated with giddiness during the day, but not at night.

Condition when examined on December 14th.

The patient is a healthy looking man. Nothing abnormal is found on examination of the chest, abdomen and nervous system. His response to exercise was tested by making him walk up and down three flights of stairs in one minute. This caused much dyspnœa for some minutes, although the pulse returned to its original rate within ¾ minute, and during the second minute after exercise was 48, or 16 beats below its original rate.

The significance of this bradycardia* is not known, but in this case it was certainly not a sign of well-being. (See Table 45.) The degree of dyspnœa was estimated by making the patient breathe through a meter on his return, and measuring the amount of expired air every minute; during the first 6 minutes after the exercise he expired 88 litres. (A normal subject expired 49 litres after the same exercise.)

His red cell count was 7.53 million, and his hæmoglobin 104 per cent. (See Table 46.)

---

* Bradycardia on exercise in gassed animals (amounting to temporary stoppage) has been observed by J. Barcroft, Lewis and others (see report forwarded to R.S, War Committee, April, 1916). The bradycardia was abolished by section of the vagus nerves.

TABLE 45.—Case 12. Lt. P. Pulse-Rate after Exercise.

Before treatment, December 14th, 1917.		*After treatment, December 21st, 1917.*	
Time	Rate per Minute.	Time.	Rate per Minute.
Before exercise	64	Before exercise	58
1st ¼-minute	92	1st ¼-minute	88
2nd ,, ...	80	2nd ,, ...	72
3rd ,, ...	**64**	3rd ,, ...	**56**
4th ,, ...	60	4th ,, ...	56
5th ,, ...	48	5th ,, ...	60
6th ,, ...	52	6th ,, ...	56
7th ,, ...	52	7th ,, ...	56
8th ,, ...	48	8th ,, ...	60
		3rd minute	63
		4th ,, ...	63
		5th ,, ...	64
		6th ,, ...	56
		7th ,, ...	60
		8th ,, ...	59
		9th ,, ...	60
		10th ,, ...	62

TABLE 46.—Case 12. Lt. P. (Treatment, December 14th—21st.)

Date.	Time.	Red Cells.	Hb.
		Millions per cu. mm.	per cent.
1917.			
December 14th	10.30 a.m.	7.23	104
	6.45 p.m.	7.94	—
	9 p.m.	7.43	104
	10 p.m. (entered chamber)	—	—
,, 15th	10.30 a.m.	7.54	104
,, 16th	6 p.m.	6.29	103
,, 17th	10 a.m.	6.23	102
	3.30 p.m.	6.05	100
,, 18th	10.30 a.m.	5.69	101
	3.30 p.m.	5.05	100
,, 19th	10 a.m.	5.78	100
	5.15 p.m.	5.34	98
,, 20th	10.15 a.m.	5.46	100
,, 21st	9.15 a.m. (left chamber)	—	—
	11 a.m.	4.90	97
,, 22nd	10 a.m.	5.40	101
,, 24th	11 a.m.	5.30	99
,, 27th	2.30 p.m.	5.54	98
,, 31st	11.30 a.m.	5.54	101
1918.			
January 3rd	11.30 a.m.	6.0 (?)	102
,, 5th	10.30 a.m.	4.6	96
,, 9th	10.30 a.m.	5.25	99

Treatment.

He was put in the oxygen chamber at 10 p.m., December 14th, and remained there, with intervals for exercise, until 9.15 a.m., December 21st. He felt better for the treatment, and was able to walk faster and for longer distances. After the test exercise his dyspnœa was but little less, the amount of expired air being 81. His pulse returned to its original rate within ¾ minute, and did not fall below it as before treatment. His red cell count fell to 4.9 million, and his hæmoglobin to 97 per cent.

He was kept under observation for the next month. His red cell count varied somewhat but kept about 5.5. million with a hæmoglobin of 96 per cent. to 102 per cent. (See Table 46.) He had several boils during this time, and owing to the septic absorption from these his general condition was much impaired; further exercise tests were therefore not made.

CASE 13.—*Pte. F. Age* 21.

History previous to being Gassed.

The patient was always a healthy man, but had never done heavy work or played games since his school-days. He used to bicycle, and could ride 40 miles a day.

History of being Gassed.

He was gassed with phosgene in February, 1917, but returned to duty after three days. His immediate symptoms were vomiting, headache, cough and dyspnœa. He never felt really well afterwards, always being "short-winded." He was gassed again in July, but not sufficiently badly to make him report sick; from this time, however, his dyspnœa gradually became worse, and he went into hospital in October.

Present Symptoms.

He complains of dyspnœa on exertion, and of attacks of dyspnœa at night; these attacks occur about once a fortnight, and last about half-an-hour.

Condition when examined on December 14th.

The patient looks well. Nothing abnormal is found on examination of the chest, abdomen or nervous system. After a test exercise his pulse returned to its original rate within one minute. (See Table 47.) His expired air during the 6 minutes after exercise measured 76.5 litres, or 36 per cent. above normal, the expired air for a normal subject being 56. His red cell count was 6.41 million, and his hæmoglobin 107 per cent. (See Table 48.)

TABLE 47.—Case 13. Pte. F. (Treatment, 14th—20th December, 1917.)

Before treatment, December 14th.		*After treatment, December 20th.*	
Time.	Rate per Minute.	Time.	Rate per Minute.
Before exercise	76	Before exercise	73
1st ¼-minute	136	1st ¼-minute	112
2nd ,, ...	104	2nd ,, ...	**76**
3rd ,, ...	84	3rd ,, ...	76
4th ,, ...	**80**	4th ,, ...	68
5th ,, ...	76	5th ,, ...	72
6th ,, ...	68	6th ,, ...	60
7th ,, ...	68	7th ,, ...	60
8th ,, ...	68	8th ,, ...	56
		3rd minute	58
		4th ,, ...	65
		5th ,, ...	68

TABLE 48.—Case 13. Pte. F. (Treatment, December 14th—21st, 1917.)

Date.	Time.	Red Cells.	Hb.
		Millions per cu. mm.	per cent.
1917.			
December 14th	4 p.m.	6.25 (?)	108
	6 p.m.	6.57	106
	8.30 p.m.	—	106
	10 p.m. (entered chamber)	—	—
,, 15th	10.30 a.m.	6.37	107
,, 16th	4 p.m.	6.56	107
,, 17th	10.30 a.m.	5.75	105
	3.30 p.m.	6.16	102
,, 18th	10.30 a.m.	5.5	101
	3.30 p.m.	6.37	100
,, 19th	10 a.m.	5.80	99
	3.45 p.m.	5.65	99
,, 20th	10.30 a.m.	6.25	104
	3 p.m.	5.30	101
,, 21st	9.15 a.m. (left chamber)	—	—
,, 22nd	10 a.m.	5.97	102
,, 24th	10.30 a.m.	6.12	101
,, 27th	3.30 p.m.	6.0	102
,, 31st	11.30 a.m.	6.32	100.5
1918.			
January 9th	11 a.m.	6.48	102

Treatment.

He was put in the oxygen chamber at 10 p.m., December 14th, and remained there, with intervals for exercise, until 9.15 a.m., December 21st. He felt very much improved; his dyspnœa on exertion was much less, and no attacks at night occurred. After the test exercise his pulse fell to its original rate within half a minute (see Table 47), and the amount of expired air was 65.0 litres, or only 16 per cent. above the normal as against 36 per cent. before treatment. His red cell count fell to 5.3, and his hæmoglobin to 101 per cent. (See Table 48.)

He was kept under observation during the next month. His red cell count and hæmoglobin varied a good deal, but as a rule was about its original level; his hæmoglobin percentage was steadier, 100–102 per cent. A test exercise was given 19 days after treatment; his pulse rate fell to its original rate within one minute (see Table 49), but his dyspnœa was rather more marked, the expired air measuring 71 litres, or 27 per cent. above the normal.

TABLE 49.—Case 13. Pte. F. Pulse-Rate after Exercise.

III.—Three weeks after treatment.

Time.	Rate per Minute.	Time.	Rate per Minute.
Before exercise	92	6th ¼-minute	84
1st ¼-minute	140	7th ,, ...	88
2nd ,, ...	116	8th ,, ...	88
3rd ,, ...	96	3rd minute	93
4th ,, ...	92	4th ,, ...	93
5th ,, ...	92	5th ,, ...	96

He had had some attacks of nocturnal dyspnœa, but they were not severe.

This patient showed more tendency than any of the others to return to his original condition. He will be treated with oxygen again.

It has been suggested that the abolition of the attacks of nocturnal dyspnœa might possibly be due to the psychological effect of the chamber and the noise caused by the blowing in of oxygen. To test this the following experiment was performed. A patient subject to nocturnal dyspnœa was put in the chamber and oxygen was blown in according to the usual method; a pipe, however, through which it could escape was left open, with the result that directly after the oxygen had been let in the percentage was only 22. During the night, air flowed in through three different pipes, and the oxygen percentage in the morning was 20.5. This was done on three successive nights, and on two occasions the patient woke up feeling short of breath, and had to prop himself up in bed to obtain relief. He also said on the third morning that the treatment was not making him feel any better. Subsequently he was treated with oxygen in the usual way; he had no further attacks, and said he was much improved.

Summary.

1. The effects of treatment of thirteen cases of gas poisoning with oxygen has been described.

The treatment consisted in spending about 5 days in a chamber containing 40-50 per cent. of oxygen. The patients slept in the chamber, but came out for some hours each day for exercise.

These patients all appeared to benefit from the treatment, some of them to a remarkable extent. They felt better and were undoubtedly more capable of doing active work. A study of their symptoms, high red cell counts and hæmoglobin values, nocturnal dyspnœa and especially disordered action of the heart, showed that the men really were better.

2. The polycythæmia which often occurs after gas poisoning is abolished for a time. It tends to recur but not usually to the former level, and yields more easily to a second treatment. Oxygen treatment does not lower the blood-counts of patients not already polycythæmic.

3. The hæmoglobin is frequently somewhat diminished, but the usual tendency is for the colour-index to rise.

4. Abnormal pulse-rates are very common after gas poisoning. These fall into two principal categories :—

(*a*) The pulse is at first very rapid upon exercise, and after this the rapidity is maintained for an abnormally long time.

(*b*) The pulse is less increased in rate than normally after exercise, but it suddenly becomes abnormally, if not dangerously, slow.

Both these conditions are corrected by oxygen treatment. The benefit seems to outlast the treatment, and in fact has been maintained up to the present date in the cases observed.

5. Attacks of nocturnal dyspnœa, when present, are always abolished for a time, in many cases apparently permanently.

Further observations are being carried out, especially on the respiratory exchange and the acidosis. For the purpose of control, observations are also being made upon the effect of oxygen treatment on patients showing similar symptoms, namely, disordered action of the heart, emphysema, nocturnal attacks of breathlessness, neurasthenia and polycythæmia, but from causes other than gas poisoning.

N.B.—*The Superintendent of Experiments, R.E. Experimental Station, Porton, desires to take this opportunity of thanking the University of Cambridge for the use of their gas-chambers and for the facilities which have been afforded during the conduct of the research; also the Medical Research Committee for having defrayed a considerable portion of the expenses.*

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MEDICAL RESEARCH COMMITTEE.

War Special Report Series

REPORTS

OF THE

CHEMICAL WARFARE MEDICAL COMMITTEE.

No. 7.—CHANGES OBSERVED IN THE HEART AND CIRCULATION, AND THE GENERAL AFTER-EFFECTS OF IRRITANT GAS POISONING.

April, 1918.

In January, 1918, the Director-General, Army Medical Service, with the concurrence of the Controller of Chemical Warfare, appointed the following Committee to prepare reports, based upon information received from all sources at the Chemical Warfare Department, for submission to him with a view to their distribution to those concerned, to make suggestions for further co-ordinated medical investigations that may seem desirable, and to advise him generally in respect of the scientific medical aspects of Chemical Warfare :—

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OBSERVATIONS ON THE EFFECTS OF GAS POISONING ON THE HEART SOUNDS AND PULSE RATE IN GOATS.

By G. H. Hunt, Captain, R.A.M.C. (T.F.)
(*From the Porton Laboratories.*)

Last summer Captain R. A. Peters, R.A.M.C., called my attention to the fact that the second heart sound in "gassed" goats was frequently increased in intensity, and suggested the possible value of this sign as an indication of gas poisoning. My own experience is in accordance with his, and I agree with him that there is a *real* increase in the intensity of the second sound and not an *apparent* one due to diminution in intensity of the first sound. In support of this view is the fact that the sign occurred even in cases where the dose of gas was small and where the other signs indicated that the goat was only very slightly affected. In man a definite diminution in intensity of the first sound is nearly always associated with profound constitutional disturbance; in the lightly gassed goats there was no evidence of any such disturbance likely to cause a weakening of the first sound.

Tables Ia and Ib show the number of cases in which an increase in intensity of the second sound was observed at different times after "gassing" with phosgene or chloropicrin. It will be noticed:—

(i) That the second sound is altered both by large and small doses, and rather more often by the latter than the former;
(ii) That the sign appears within 2 hours after "gassing," persists for some hours, and then in some cases disappears.

Should the same sign be found in man—there is some evidence that this is the case—it would be of considerable value as an aid to the diagnosis of gas poisoning in the early stage, particularly in the lighter cases, where difficulty often arises.

A rise of pulse rate after "gassing" is a frequent, but not invariable, sign in goats. Table II shows the changes in pulse rates at different periods following large and small doses. It will be noticed that the increase in pulse rate is less when the dose is small. The pulse rates were taken from the carotid artery in most cases; in a few by auscultation or palpation of the heart. In order to avoid the effect of previous muscular exertion no pulse rate was taken until the goat had been tethered for at least 10 minutes. It is more difficult to avoid the effect of excitement, but a goat will generally remain quiet if approached in a conciliatory manner; it is possible, however,

that the occasional fall in pulse rate after "gassing" (*e.g.*, in experiments 1, 7, 8, 13) is due to the animal's greater nervousness at one time than another.

TABLE IA. (Large dose.)

	Sign Present.	Sign Absent.	Percentage Present.	Percentage Absent.
Time of gassing to 2 hours ...	86	23	78·9	21·1
2–6 hours	70	21	77·0	23·0
6–8 „	16	3	84·2	15·8
16–24 „	20	13	60·6	39·4
24–48 „	5	6	45·4	54·6
48 72 „	2	2	50·0	50·0

TABLE IB. (Small dose.)

	Sign Present.	Sign Absent.	Percentage Present.	Percentage Absent.
Time of gassing to 2 hours ...	7	1	78·9	21·1
2–6 hours	92	14	77·0	23·0
16–24 „	25	11	69·4	30·6
48–72 „	4	3	57·1	42·9

TABLE II.

"S" indicates that the dose given was small; "L" that the dose was large.

Experiment No.	Time after Gassing.	Alterations in Pulse-rate per Minute.
1. L. ...	1 hour ...	−4, 52, 0, 8, 32, 4, 56, 58. (Average 25·75.)
2. L. ...	6 hours ...	58, 60, 56, 12, 16, 8, 72, 20, 32, 16. (Average 35.)
3. S. ...	6 „ ...	0, 4, 12, 37, 0. (Average 10·6.)
	24 „ ...	12, 36, 12, 36, 30. (Average 25·2.)
4. L. ...	16 „ ...	12, 32, 24, 38. (Average 26·5.)
	40 „ ...	56, 68, 42, 44. (Average 52·5.)
5. L. ...	24 „ ...	16, 20, 48, 8, 36, 108, 48. (Average 40·6.)
6. S. ...	4½ „ ...	20, 4, 12, 24, 32, 0, 20, 24, −16, 0. (Average 12.)
7. L. ...	¼ „ ...	16, −4, 16, 54, 36, 12, 4, 0, 32, −4. (Average 16·2.)
8. L. ...	5¼ „ ...	20, 10, 58, 8, −4, 16, 34, 0, 48, 40. (Average 23.)
9. L. ...	3 „ ...	4, 0, 20, 34, 20, 20, 32, 42, 24, 6, 42, 26, 12, 28. (Average 22·1.)
10. L. ...	4¼ „ ...	0, 36, 34, 0, 14, 20, 34, −8. (Average 16·25.)
11. L. ...	¼ hour ...	38, 12, 12, 28. (Average 22·5.)
	6½ hours ...	50, 36, 42, 52. (Average 45·0.)
	22 „ ...	70, 20, 4, 56. (Average 37·5.)
	48 „ ...	80, 2, 16, 12. (Average 27·5.)
12. S. ...	5¼ „ ...	26, 10, 12, 0, 20. (Average 13·6.)
	23 „ ...	14, 20, 28, 44, 32. (Average 27·6.)
	70 „ ...	30, 52, 52, 8. (Average 35·5.)
13. S. ...	3 „ ...	4, 0, 13, −16, 12, −2, 12, 20, −8, 6, 22, 24, 12, 4. (Average 7·4.)

CHANGES OBSERVED IN THE HEART AND CIRCULATION AS A RESULT OF GAS POISONING.

By R. A. Peters, Captain, R.A.M.C.

(*From the Porton Laboratories.*)

The changes observed in the heart and circulation both in gassed animals and in gassed men are as follows :—

I. *Immediate effects.*

(1) Quicker heart beat in the early stages (primary tachycardia).

(2) Accentuated second cardiac sound.

(3) Cardiac dilatation (right-sided).

II. *Remote effects.*

(1) Tachycardia.

(2) Left-sided dilatation (rare).

They vary in severity according to the nature of the gassing, and can only be taken as applicable to the class of lung irritants. The effect of A.C. upon the heart will be appended in a brief note.

Evidence is accumulating to show that the immediate changes after gassing are, in the main, secondary to the condition of the lungs, and are due :—

(*a*) To increased resistance in the lung ; and

(*b*) To oxygen want.

Both (*a*) and (*b*) may be explained by the gradual development of inflammation in the lung. It is not yet proved, however, that the irritation of the respiratory passages does not set up some contraction of the bronchial musculature (bronchial spasm).

The chief clinical and experimental evidence available as to the presence of the above changes will be taken in order. Further evidence shows that these changes may be either abolished or diminished by treatment with oxygen. This emphasises the importance of oxygen treatment, and supplies further ground for the belief that the changes are mainly due to the condition of the lungs.

I. Immediate Effects.

1. *Primary Tachycardia.*

The evidence for its appearance is :—

(1) *Experimental.*—The following rises in pulse rate have been observed at Porton in gassed goats.*

Gases : Phosgene and Chloropicrin.

Experiment.	Dose.	No.	Time after Gassing.	Alterations in Pulse-rate Per Minute.
1	Large ...	8 goats ...	1 hour ...	—4, 52, 0, 8, 32, 4, 56, 58.
2	Large ...	10 „ ...	6 hours	58, 60, 56, 12, 16, 8, 72, 20, 32, 16.
3	Small ...	5 „ (mild gassing)	6 „	0, 4, 12, 37, 0.
			24 „	12, 36, 12, 36, 30.
			16 „	12, 32, 24, 38.
4	Large ...	4 goats	40 „	56, 68, 42, 44.
5	Large ...	7 „ ...	24 „	16, 20, 48, 8, 36, 108, 48.

(Bracketed numbers are pulse rates for the same goats at different times.)

In all cases except four, —4, 0 (Experiment 1), 0, 0 (Experiment 3), there has been a rise of pulse rate, in some cases considerable.

(2) *Clinical.*—There is a considerable amount of evidence from France to show that the tachycardia exists. Captain Douglas has collected a mass of evidence illustrating this, but only a few cases will be quoted.

(*a*)† No. 44352, Pte. G. Gassed 6 a.m. Sixteen hours after gassing, pulse was impossible to count. Bad case.

(*b*)‡ No. 130170, Pnr. C. Three hours after gassing, pulse 100. Mild case.

(*c*)§ No. 130122, Pnr. P. Twelve hours after gassing, pulse 132. Mild case.

(*d*)**V. Ten hours after gassing, pulse 144.

The evidence for the absence or reduction of primary tachycardia by treatment with oxygen is also good.

(1) *Experimental.*—Two experiments were made at Porton on goats, one of which (Experiment A) is reported in C.C.P. 1602. In each of these experiments a pair of animals was gassed, one was used

* Hunt, R.A.M.C. (*C.C.P.* 3641, *Porton Reports*).
† C. G. Douglas, R.A.M.C., Central Laboratory, G.H.Q.
‡ R. A. Peters (*Special Brigade R.E. Reports, First Army*).
§ Ogdin March (*C.C.P.* 1602, *Porton*). Also Paper by McNee (*G.H.Q. Report*).
** Adrian Stokes (*D.G.S. Reports*).

as control and the other treated with oxygen. Both the animals treated with oxygen had a considerably lower pulse rate than the control over the first six hours after gassing. In the first experiment, A, the lower pulse rate remained for some time after gassing, three weeks. In Experiment B the results were complicated by secondary infection.

The experiments are being repeated on a larger scale.

(2) *Clinical.*—In case (*a*) referred to above.

Oxygen treatment with the Haldane apparatus brought the pulse rate down as follows, from a pulse impossible to count at 16 hours :—

To 19 hours after gassing	..	..	Pulse 112.
,, 21	,,	,,	,,	..	..	,,	108.
,, 28	,,	,,	,,	..	..	,,	100.

In case (*b*). Immediately after giving oxygen to 78.

In case (*c*). An officer gassed at the same time as Pnr. P., but more severely, was treated with oxygen with the Haldane apparatus from one hour after gassing.

He never had a pulse rate over 100.

Case (*d*). From pulse 144, 10 hours after gassing, pulse came down as follows :—

19 hours after gassing	..	..	Pulse 120.
21 ,,	,,	,,	..	..	,, 112.

Other instances could be given, but the above illustrates clearly that the initial tachycardia is associated with oxygen want, and can be helped by giving oxygen.

NOTE.—A *slow* heart beat is sometimes found in gassed patients in C.C.S. The beat is slow, but is accelerated by the mildest exercise. The patient is not usually suffering from obvious oxygen want. From the cases of Cpl. S.,* Pnrs. C. and P. and Lieut. McL., it is clear that oxygen want appears early.

Therefore it is quite possible that during the six to nine hours previous to admission the patient has suffered from oxygen want for part of the time. The slow heart beat is perhaps the mark left by this oxygen want.

2. *Accentuated Cardiac Second Sound.*

The evidence for its appearance is both

(i) *Experimental.*—At Porton, practically all gassed goats develop it at some period. It appears more frequently with small than large doses (G. H. Hunt).

It is found at anything from 1 to 72 hours after gassing. Two tables are sufficient to illustrate this.

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*Teague, R.A.M.C. (*Special Brigade Reports, First Army*).

(From C.C.P. 1923 [continuation of C.C.P. 1602].)

Occurrence of Accentuated Second Heart Sound.

Experiment B. (*See above.*)

(1/12,000 *Phosgene for* 8 *Minutes.*)

Time after Gassing.	Occurrence of Accentuated Second Sound.		Remarks.
	Oxygen Goat.	Control Goat.	
4 days	No accentuated second sound	Accentuated second sound	

Experiment C.—Gas Phosgene.

1 hour	Slight accentuated second sound	No accentuated second sound	
1 „	—	—	Oxygen begins.
1 hour 35 mins....	—	No accentuated second sound	
2 hours	—	Slight accentuated second sound	
5 „	Slight accentuated second sound	Marked accentuated second sound	
10 „	Slight accentuated second sound	Marked accentuated second sound	Oxygen stopped.
20 „	No accentuated second sound	Marked accentuated second sound	
3 days	No accentuated second sound	No accentuated second sound	

Experiment D.—Gas Phosgene.

1 hour	Sounds very difficult to hear	No accentuated second sound	
1 „	—	—	Administration of oxygen commences and is given continuously till hours after gassing. Then stopped occasionally for 10 minutes.
1 hour 35 mins. ...	Sounds very difficult to hear	Slight accentuated second sound	
5 hours	Sounds very difficult to hear	Marked accentuated second sound	
9 hours 30 mins.	Sounds easily heard	Marked accentuated second sound	Oxygen stopped.
12 „ 20 „ ...	No accentuated second sound	—	
18 hours (about)	No accentuated second sound	Dead	
19 „	No accentuated second sound	—	
1 day	No accentuated second sound	—	
2 days	No accentuated second sound	—	

*Gases : Phosgene and Chloropicrin.**

*Table I*A. (*Large dose.*)

	Sign Present.	Sign Absent.	Percentage Present.	Percentage Absent.
Time of gassing to 2 hours...	86	23	78·9	21·1
2–6 hours	70	21	77·0	23·0
6–8 ,, ...	16	3	84·2	15·8
16–24 ,, ...	20	13	60·6	39·4
24–48 ,, ...	5	6	45·4	54·6
48–72 ,, ...	2	2	50·0	50·0

* Captain Hunt (C.C.P. 3,641.)

*Table I*B. (*Small dose.*)

	Sign Present.	Sign Absent.	Percentage Present.	Percentage Absent.
Time of gassing to 2 hours...	7	1	78·9	21·1
2–6 hours	92	14	77·0	23·0
16–24 ,, ...	25	11	69·4	30·6
48–72 ,, ...	4	3	57·1	42·9

And (ii) *Clinical.*—It has been observed repeatedly by Captain Teague,† No. 1, C.C.S., who used it as a means of determining whether a man complaining of gassing in the trenches was really gassed or not.

Evidence for Removal by Oxygen Treatment.

Experimental.—There is experimental evidence to show that oxygen relieves this symptom in gassed goats.

Clinical.—In Lieut. McL.'s case it never appeared, nor did it appear in cases of Pnr. C. and Pnr. S., mentioned in the account of primary tachycardia.

A discussion of the meaning of this physical sign must be taken with :—

3. *The Right-sided Dilatation of the Heart.*

The experimental evidence here is necessarily poor, because it is almost impossible to percuss a goat's heart accurately.

The clinical evidence is abundant. A number of cases examined at No. 1 C.C.S. showed this sign,‡ sometimes the heart border being as much as 1 inch to the right of the sternum. The cases examined were mostly within the first 24 hours of gassing.

† Some notes on the early diagnosis of slight cases of Phosgene poisoning. (*G.H.Q. Reports*).

‡ Teague, R.A.M.C., *No.* 1 *C.C.S.*

The cases of Pnrs. C. and S., referred to above (under primary tachycardia) also showed right-sided dilatation within seven hours, and in these cases the dilatation disappeared under oxygen treatment within 24 hours.

N.B.—As a remote sign, right-sided dilatation was only found in 1 per cent. of cases at Hardelot.*

II. Remote Effects.

1. *Tachycardia.*

With this there are included both the tachycardia occurring within the week after gassing, and the later tachycardia after the lungs are apparently normal.

It may be discussed under the following heads :—

(*a*) Tachycardia at rest.
(*b*) Tachycardia upon exercise.

Evidence for the presence of :—

(*a*) *Tachycardia at rest.*

Experimental.—Many of the goats at Porton† after recovery show an increased pulse-rate of from 10–30 while at rest.

Clinical.—A number of gassed soldiers may recover and have pulses persistently above 80, and in some cases pulses of 100.‡

(*b*) *Tachycardia upon exercise.*

This manifests itself in two ways.

The pulse (i) rises more than the normal pulse for a given amount of exercise ;
(ii) returns to the normal more slowly after exercise.

Experimental.—At present the evidence is scanty, and is confined to (i). In the control goat referred to above (C.C.P. 1923), there was a marked tachycardia upon exercise for several weeks after gassing. This has also been observed in other goats at Porton.

Clinical.—Both (i) and (ii) were observed in 116 out of 320 gassed soldiers at Hardelot.§

The evidence for the prevention or alleviation of these after-effects by treatment is at present small,‖ and is confined to the effects of early oxygen treatment.

Experimental.—Of the goats referred to in C.C.P. 1923, Experiment A, the goat treated from one hour after gassing with oxygen

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* Hunt and Price Jones (*G.H.Q. Report*).
† Hunt (unpublished reports).
‡ Hunt (Hardelot cases).
§ Hunt and Price Jones. Later effects of poisoning by asphyxiating gas (*G.H.Q. Report*).
‖ Experiments bearing upon this are already in progress at Porton.

has never had either (*a*) or (*b*), both of which were shown by the control. The oxygen goat is still alive (three months after gassing), and is one of the most fit goats on the farm. (Two other goats similarly treated show every sign of health.)

Clinical.—More recently, Captain Hunt treated a case of a gassed man who had tachycardia and nocturnal dyspnœa with four days' exposure to 35–45 per cent. oxygen in the gas chamber at Cambridge. Since the time of treatment, *i.e.*, for three weeks, this man has shown a very considerable improvement as regards the tachycardia and nocturnal dyspnœa. The action of the oxygen in this case is obscure.*

2. *Left-sided Dilatation of the Heart.*

This was found in 5 per cent. of the cases of gassed soldiers at Hardelot.†

NOTE.—*Condition of the heart after exposure to Prussic Acid or mixtures containing Prussic Acid.*

So far there have been no recorded observations on men. In some of the trench shoots at Porton, goats have been made unconscious. In this condition they lie on the ground gasping for periods of one hour or more.

Pulse rates are invariably raised. Instead of the normal 80–90, they have been found 160–230. Two cases will be given in illustration :—

Goat 92 ..	Unconscious after shoot. One hour after, pulse 230. Next morning, pulse 108.
Goat 111..	Unconscious after shoot. One hour after, pulse 180. Six days after, pulse 144.

When these animals recover, their pulses have shown a tachycardia, and there is often some irregularity of the heart beat.

THE AFTER-EFFECTS OF IRRITANT GAS POISONING.‡

By JOHN C. MEAKINS, Lieut.-Colonel, C.A.M.C., and
T. W. WALKER, Captain, C.A.M.C.

(*From the Medical Clinic of No.* 15 *Canadian General Hospital, Taplow, Bucks.*)

The present report is based on cases of irritant gas poisoning admitted to this hospital between July 1st and December 31st, 1917. It was deemed advisable to exclude any cases in which the character

* This work has been substantiated by further experiment.

† Hunt and Price Jones.

‡ An investigation undertaken on behalf of the Medical Research Committee.

of the gas was uncertain. Therefore a certain number have had to be eliminated, as it was difficult to determine from the history of certain of these cases what gas was responsible for the symptoms. In all, 200 cases have been analysed. They consist of the following:—

Dichlorethyl sulphide $(C_2H_4Cl)_2$ S (mustard gas) ..	163
Phosgene ($COCl_2$)	33
Chlorine	4

The average period before being admitted to this hospital was 14 days. Many of the cases were admitted during the first week, while a number had been retained in hospital in France for a considerable period on account of the severity of their symptoms (Table 5). The present report deals with the principal late symptoms, the chief causes preventing their return to a normal state of health, and the treatment of the conditions. Finally, we discuss the importance of irritant gas poisoning in affecting the future usefulness of the soldier.

The chief forms of irritating gases used by the enemy are of two main varieties : Suffocative and vesicant. Typical examples of the suffocative group are phosgene and chlorine, while dichlorethyl sulphide or "Mustard Gas" (so called on account of the odour) is the only vesicant so far used. The suffocative gases act mainly on the alveolar epithelium of the lungs, causing acute pulmonary œdema of very rapid onset and thrombosis of the pulmonary capillaries. In consequence of the œdema of the lungs during the early stage, deficient oxygenation of the blood occurs, unless prevented by the administration of oxygen. This deficient oxygenation gives rise to widespread temporary injury in various systems of the body.

The only vesicant hitherto employed is dichlorethyl sulphide, an oily liquid used in shells and scattered from them on the ground, where it slowly evaporates. This not only exposes those in the immediate vicinity of the shell-burst, but may also affect those who walk over the contaminated ground later. Thus it may be difficult to obtain a definite history as to the exact time when the patient was subjected to this gas. The fluid may be scattered also on clothing, shell-casings, rifles, etc., and may thus become effective through direct contamination of the skin. The main action of this substance is irritant on the skin. eyes, and respiratory passages. The ulceration of the mucous membrane of the air passages may be so extensive and severe as to cause death *per se* or a fatal result may be the consequence of the later development of broncho-pneumonia. There has evidently been in a certain number of the severe pulmonary cases an interference with the proper oxygenation of the blood, which may give rise to widely spread temporary lesions as in the suffocative group.

Symptoms.

The chief symptoms which were complained of during the period of observation at this hospital are set forth in Table 1. Apart from the symptoms caused directly by the irritative action of the gases, there is a distinct group of great importance, which occurs after both forms of gas poisoning, but most commonly after phosgene. These symptoms are commonly regarded as constituting the condition of

disordered action of the heart (D.A.H., or the "Effort Syndrome"). They consist chiefly of dyspnœa, præcordial or chest pain, palpitation, fatigue, dizziness and even syncope. The degree of predominance of any of the symptoms varies with the individual. The patient complains frequently of disturbed sleep varying in degree. This may be characterised by dreams, paroxysms of coughing, starting awake with a feeling of pressure on the chest, and even acute attacks of dyspnœa with orthopnœa. There are also various nervous symptoms of a "functional" character, closely associated with this symptom-complex. For convenience, the symptoms common to all three forms of gas poisoning are taken together and analysed.

In nine cases (six mustard gas and three phosgene) there were no symptoms when the patients came under our observation. In all the other cases, symptoms were present.

TABLE 1.

Symptoms.	Mustard Gas.		Phosgene.	
	No.	Per cent.	No.	Per cent.
Cough	88	54	8	24
Pain in chest	79	48	20	60
Dyspnœa	68	42	28	84
Râles	49	30	10	30
Conjunctivitis	52	32	—	—
Laryngitis	29	18	—	—
Burns	37	23	—	—
Abdominal pain	25	15	—	—
Dizziness	19	12	8	24
Tachycardia	14	9	8	24
Expectoration	17	10	1	3
Vomiting	13	8	2	6
Painful micturition	12	7	—	—
Fatigue	12	7	12	36
No complaints	6	4	3	9

Dyspnœa.—This was one of the most common symptoms, and exerted great influence in retarding the patient's recovery. In both mustard gas and phosgene poisoning there was frequently a history of dyspnœa from the early stages of gassing. This was particularly the case in those who had been subjected to phosgene, and the persistence of this symptom was more frequent after this gas. As will be seen in Table 1, it occurred in 84 per cent. of the phosgene cases, and in 42 per cent. of the mustard gas cases. While under our care the dyspnœa was manifested in different ways. A considerable number of cases complained of difficulty in breathing, and had rapid respirations even when at rest. This was more common in those affected by mustard gas. The most striking characteristic of the breathing was its shallow nature. It was not unusual to find the volume of tidal air reduced to 150 or 200 cc., per respiration, when at rest. The pulmonary ventilation was therefore augmented by increas-

ing the respiratory rate to a conspicuous degree. These patients could not increase, voluntarily or involuntarily, the *volume* of their respirations beyond a limited extent, with the result that the slightest exertion produced a greatly increased *rate*. This abnormal type of breathing was found to be of great importance in the causation of other symptoms. A full description and investigation of this condition will be the subject of a later communication.

The occurrence of pain and the ready production of coughing by taking a deep breath was a conspicuous factor in making satisfactory breathing difficult. This was apparently the result of the local action of the mustard gas on the upper respiratory passages. The relationship between the frequency of chest pain and cough in these cases will be dealt with later. Although dyspnœa occurred very frequently after phosgene poisoning, it was less complained of *at rest* than after mustard gas. (See Table 2.) All the cases which had dyspnœa when at rest, naturally complained of it also on exertion. In addition a large number (particularly of phosgene cases) had dyspnœa only on exertion. All of those who had dyspnœa while at rest, would, after improving, be dyspnœic only on exertion. The dyspnœa on exertion was a very distressing symptom, incapacitating the patient at times from taking any exercise, even to walking. There were a certain number of cases of dyspnœa at night. These all complained of it during the day, sometimes when at rest, and always on exertion. This form was also more common in the phosgene cases. It occurred either as an increased difficulty of breathing when in the recumbent position, or what was more common, as paroxysms during sleep. When this occurred the patients would awake suddenly with a feeling of intense distress, almost of suffocation, which would necessitate their sitting up in bed in order to obtain relief. The importance of this form of dyspnœa in the physiology and treatment of the condition will be dealt with later.

Associated with the dyspnœa in varying frequency there was tachycardia, dizziness and fatigue (see Table 1). These symptoms were all more frequent in the phosgene cases. They never occurred without dyspnœa. On exertion they were much more frequent, but were very variable in so far as their degree was concerned. These were the cases which exhibited the typical symptoms of disordered action of the heart (or effort syndrome).

TABLE 2.

Type of Dyspnœa.	Mustard Gas.		Phosgene.	
	No.	Per cent.	No.	Per cent.
On exertion only	31	46	19	68
At rest by day	37	54	9	32
By night, usually paroxysmal ...	7	10	10	36

Cough.—Cough was the most common symptom in the cases of mustard gas poisoning. It varied in degree from a mild barking type to an extreme paroxysmal variety which would cause the patient to become cyanosed, acutely dyspnœic, and extremely exhausted. It was usually accompanied by expectoration. Occasionally it was so severe as to produce slight hæmoptysis. The most frequent type was of a dry ringing character, as if due to irritation of the larynx, or the larger bronchi. In the early stages of irritant gas poisoning there is undoubtedly considerable expectoration, but by the time the patients have arrived in the United Kingdom this has greatly diminished, until it is usually a comparatively insignificant symptom, especially in phosgene poisoning. The occurrence of paroxysmal cough at night is very important and closely connected with nocturnal dyspnœa. Those who had this form of nocturnal cough would not, as a rule, complain of nocturnal dyspnœa, as the dyspnœa was masked by the coughing. But it seemed clear that the cough was initiated by unconsciously trying to take a deep breath in order to overcome the increasing deficiency of oxygen which occurred during sleep. Apparently the cough and dyspnœa were manifestations of the same condition. In those who were prone to cough on breathing deeply, there was a greater likelihood of their night's rest being disturbed by paroxysms of coughing. If an attack of nocturnal dyspnœa should occur, the patient immediately attempts, even before fully awake, to overcome this with deep inspirations, which precipitates a violent attack of coughing, in which the dyspnœa is obscured, and the patient complains later only of the cough. In those cases where the physical signs in the chest are comparatively few and the sputum scanty, the cough, if present, is more distressing than when the sputum is fairly profuse.

TABLE 3.

Character of Cough.	Mustard Gas.		Phosgene.	
	No.	Per cent.	No.	Per cent.
Slight	43	49	4	50
Severe	15	17	1	12·5
Nocturnal	30	34	3	37·5

Pain.—Pain is one of the earliest and most distressing symptoms. After the acute stage of the gas poisoning has passed it remains to a varying degree. It occurs more frequently after phosgene than after mustard gas, but differs in character in these two conditions. The patients may complain of either general pains in the chest or may localise them in the left breast. The generalised chest pain was more common after mustard gas. (See Table 4.) In these cases it was usually felt in both sides of the chest and behind the sternum. It was more or less constant and was distinctly increased by attempts to make a deep inspiration or expiration.

Either act, if beyond certain narrow limits, would usually produce a paroxysm of coughing, apparently started by the pain. It was of a dry, raw character, and situated across the upper part of the chest. In some cases it would also be felt over the lower ribs in the flanks. The pain not only produced coughing, but this in turn aggravated it. Exertion would not increase it if the demand for an increased volume of inspirated air were slight. If, however, the exertion was sufficient, the pain was much aggravated and a paroxysm of coughing usually resulted. This pain had practically disappeared after the patient had been resting quietly for a short period.

The pain localised to the left breast, or the præcordial pain, was most common after phosgene poisoning. In these cases the pain was generally localised over the left side of the chest anteriorly. It sometimes extended to the axillary region and occasionally it was felt down the inside of the left arm. Deep breathing might increase its severity, but not to the same extent as it did the chest pain. It seldom produced the paroxysms of coughing as described above. This præcordial pain was of a cramp-like character, and frequently was alarming to the patient, giving him a sensation of apprehension, even of fear. It was likely to be greatly aggravated by exertion, independently of deep breathing. When it occurred it was more or less constant for considerable periods, and might be very acute even when the patient was completely at rest. Apart from the chest pain, the skin over the site was usually extremely hyper-sensitive, with a definite area of hyperalgesia. This is the type of pain which is so intimately connected with D.A.H. or the effort syndrome.

TABLE 4.

Character of Pain.	Mustard Gas.		Phosgene.	
	No.	Per cent.	No.	Per cent.
Chest pain	54	68	5	25
Præcordial pain	25	32	15	75

Sputum.—There was a history in practically all of the mustard gas cases of early expectoration, but this had disappeared in many of them when they came under our observation. When the patients were admitted to this hospital, sputum was usually scanty in amount and not at all in proportion to the degree of cough. In fact, in many cases with very violent coughing attacks there was little or no sputum. It was quite evident that in the large majority of cases the sputum was the result of a violent attack of coughing, and not the cause. In 16 cases (10 per cent.) there was a considerable quantity of sputum. In all of these there was distinct evidence of bronchitis. The sputum was muco-purulent, and sometimes blood-streaked. In three cases the sputum was very copious; in one, amounting to 32 ounces in 24 hours. In this case bronchitic plugs were repeatedly demonstrated.

In nearly all the cases with considerable sputum the history pointed to particularly severe involvement of the air-passages during the acute stage.

In the phosgene cases there was expectoration in only one case. The œdema fluid had been almost completely absorbed in these before entrance to this hospital.

Bronchitis.—The signs in the lungs when the cases came under our observation were quite in accord with what would be expected, considering the action of the different gases. In the mustard gas cases 49 (30 per cent.) showed large moist and dry râles, indicative of involvement of the large air-passages. Very seldom were crepitations found. In the phosgene cases on the other hand the chief pulmonary signs were fine crepitant and sibylant râles, such as would indicate involvement of the smallest bronchioles and alveoli. This occurred also in 30 per cent. of the phosgene cases. In all cases the distribution of the râles was irregular, in fact patchy, the apices being most frequently involved.

During the very late convalescence of cases of irritant gas poisoning an asthmatic like condition of the lungs developed in six cases (three mustard gas and three phosgene) while under our observation. All of these exhibited severe symptoms of disordered action of the heart (effort syndrome) when first admitted, and there were no signs of pulmonary disturbance. After a few months, however, they all developed paroxysms of dyspnœa and cough associated with rapid respirations, and their lungs were full of numerous moist and dry râles. There was no evidence of bronchial spasm. Each paroxysm would last for a number of hours, and between times the lungs would be comparatively clear. The paroxysms were more prone to occur during the night. In several of the cases bronchiolitic plugs were found in the sputum occurring with the paroxysms. They were not the typical spirals of asthma, but consisted of a central core of dense mucus with a less dense periphery, mixed with many leucocytes. The importance of this late development of bronchial disturbance will be referred to later.

Larynx.—When the cases of mustard gas came under our observation there was evidence of some involvement of the larynx in a large number of cases. This varied from a slight huskiness of the voice to complete aphonia. The mild cases greatly predominated, and no recognition was taken of this symptom for very specific reasons. In 28 cases (17 per cent.) there were well-marked symptoms of laryngeal involvement—particularly pain and aphonia. But in practically all of these the severity and duration of the symptoms was out of all proportion to the amount of abnormality revealed by examination of the larynx. Unless there was direct evidence of definite involvement of the mucous membrane or the vocal cords the condition was considered to be functional. In many cases of severe hoarseness and in practically all cases of aphonia under our care due to gas poisoning there was a functional paresis of the vocal cords. Persistent lesions of the naso-pharynx were rare.

Eyes.—Conjunctivitis of a definite character occurred in 52 cases (32 per cent.). This was characterised by photophobia, injection, a

semi-purulent discharge, and slight swelling of the eye-lids. In a few cases these symptoms were extreme. But in the majority they were mild in type. Corneal complications were rare. A history of severe involvement of the eyes was, however, frequent. With a few days' rest and treatment the signs of acute inflammation soon completely disappeared. In many of the cases there was a good deal of irritation, which excited the patients to rub the eyes. This invariably aggravated the condition, and could usually be detected by the ocular conjunctiva being red in its lower part while remaining white above. Photophobia and blepharospasm were very frequent after all evidence of the inflammatory process had subsided. This was comparable to the functional laryngeal symptoms.

Skin.—Only in cases due to mustard gas poisoning was there any disturbance of the skin. This varied from a simple erythema to extensive ulceration. A number of cases continued to develop blisters for some weeks after admission to this hospital. In these cases they were usually superficial. The principal parts involved were the groins, genitals, chest, back, and flexor surfaces of the joints. The face was seldom involved, but no part was necessarily exempt. In the various parts not burnt, a brownish staining might be present, lasting for several weeks. and was accompanied by desquamation. This did not give the patient any discomfort.

Gastro-intestinal System.—(*a*) Pain. Epigastric pain was frequent in mustard gas poisoning in 25 cases (15 per cent.). It was always situated above the umbilicus, and the painful area frequently coalesced with that of the chest or præcordial pain. It was usually increased by the taking of food.

(*b*) Vomiting. A history of vomiting during the early stages was almost constant in mustard gas poisoning, and less frequent with phosgene. In a certain number of cases this persisted in both these forms of gas poisoning (mustard gas 8 per cent., phosgene 6 per cent.). It always occurred shortly after the taking of food, but was not constant in its occurrence. The vomitus was usually small in amount and contained considerable mucus, but very little food. It was as a rule very weakly acid. There was little or no nausea accompanying it, and it seemed to be more the result of a regurgitation than frank vomiting. The gastric contents after a test meal were normal in quantity. There was usually considerable mucus, and never any blood. The reaction was faintly acid, and in no case was free hydrochloric acid present. On X-ray examinations with bismuth meals the shape, size, and motility of the stomach and duodenum were normal in all the cases examined. Excitement and worry usually increased the frequency of the vomiting, even after long periods of freedom from it.

(*c*) Diarrhœa. This was not at all common, and when it did occur was usually of short duration and not prone to recur. In one case there was melæna at the time of admission to hospital, which disappeared in a few days. In another case the least excitement produced a sudden nervous diarrhœa which would last for several hours.

Genito-Urinary System.—Painful and frequent urination occurred in 12 of the mustard gas cases (7 per cent). It was described by the patient as being of a burning character, felt along the course of the

urethra during micturition. In these cases there was also frequency of urination. The amounts voided were usually small, and in several cases there was quite acute pain in the supra-pubic area at the end of micturition. In none of these cases was there any evidence of a urethral discharge.

The urine contained a trace of albumin in 8.5 per cent. of the cases. This was always of a transitory nature and was not more frequent after gas poisoning than in the ordinary cases in the medical division, apart from those suffering from nephritis. In two cases (1 per cent.) casts were found in the urine. In none of the cases with painful and frequent urination was there any abnormality of the urine to account for this.

In cases recovering from gas poisoning there is present in a varying degree a distinct neurotic element. This is usually in proportion to the severity of the exposure, but not necessarily so, as some cases which have been but lightly gassed may show neurotic symptoms to a conspicuous degree. The cause of these symptoms is not quite clear. A probable explanation may be found in the condition present in the acute stages. Cases of phosgene poisoning are most liable to these neurotic symptoms. The action of phosgene is directly on the alveolar epithelium of the lungs, causing an acute pulmonary œdema. Consequent to this, acute "oxygen want" or deficient oxygenation of the blood occurs, which gives rise to wide-spread temporary injury in various systems of the body, and particularly in the nervous system. In a certain number of the mustard gas cases there is also considerable involvement of the respiratory passages. Further, these cases suffer a great deal of chest pain during the acute stages, which interferes with deep breathing. As a consequence the respirations are shallow even though not greatly increased in rate. This is productive of "oxygen want" with all its attendant consequences. The mental effect of gas poisoning apart from the direct action cannot be ignored in the production of these neurotic symptoms. The delayed action of certain gases and the frightful consequences of high concentrations are deeply impressed upon the minds of the soldiers by the observation of their more unfortunate comrades. It has been frequently observed that soldiers will report sick with the complaint of having been gassed even when the concentration of the gas to which they have been exposed has been very dilute and the consequent effects negligible or nil.

Treatment.—When the cases arrived under our observation, the more acute symptoms of the local action of mustard gas had subsided. These symptoms are the direct results of an irritative substance, and such results are associated in some cases with secondary infection. Therefore soothing treatment is indicated.

In the mild burns without infection simple boracic ointment was found to be efficacious. The deep burns were practically always infected. They were very painful and slow of healing. Hot boracic fomentations gave great relief, and quickly overcame the secondary infection. When the burns were severe and extensive it was found necessary almost totally to submerge the patients in hot alkaline baths with the dressings in situ. In a few minutes these would become

completely soaked and would float off. The patient was left in the bath for 20 to 30 minutes. This was very soothing. It promoted cleansing of the infected areas, and was repeated twice a day, followed by liquid paraffin as a protective dressing.

In cases with a sub-acute conjunctivitis, protection of the eyes from light by a shade or dark glasses may be necessary. For the irritation warm alkaline irrigation of the conjunctivæ followed by the instillation of a drop of liquid paraffin four times a day was found to be sufficient.* The most troublesome after-effects of the conjunctivitis were photophobia and blepharospasm. These required firm treatment. When the conjunctivitis had disappeared eye shades and dark glasses were prohibited, and the patient was reassured that no damage to the eyes had resulted. A certain number of cases aggravated this condition by rubbing the eyes. It was found to be most important that this should be firmly corrected. As soon as swelling of the conjunctivæ has subsided and any corneal affection is cured mild astringents are advisable.

There were no cases where the nose or naso-pharynx were involved to an appreciable degree. The larynx, however, frequently showed swelling of the artyeno-epiglottic folds. The deficiency of approximation of the vocal cords was never great, and was usually due to swelling of the mucous membrane and slight paresis of the laryngeal muscles. In no cases was there sufficient local disturbance to account for pronounced and prolonged aphonia. When this occurred it was invariably of a neurotic origin and required appropriate treatment. This was always readily accomplished by suggestion and encouragement. Articulation exercises were very helpful.

There was sometimes bronchitis with or without a history of broncho-pneumonia. These cases required careful handling, in that too prolonged rest in bed was apt to increase and continue the neurotic elements. It was found advisable that all cases without temperature should be out of bed, dressed in their hospital clothes, in a wheel chair if necessary, and encouraged to mix with the other patients in the open air. Finally they were induced to walk as soon as possible in order that they might regain their strength and confidence.

The gastric symptoms were most refractory to treatment. They were undoubtedly neurotic, and when apparently cured would relapse just before discharge from hospital. Rest in bed was undoubtedly harmful. Occupation with physical training in the mild cases was most effectual. In the more resistent cases gastric lavage every morning, with dilute hydrochloric acid (mm XX) in water after meals, was very helpful. Occasionally it was necessary to put these patients to bed for a few days on a milk diet, but in spite of all treatment these symptoms were frequently most persistent. Their recurrence, which happened even after the patient had been discharged, was especially striking, and this frequently necessitated re-admission to another hospital for exactly the same symptoms. The pain and frequency of micturition and the albuminuria quickly cleared up without any treatment beyond increased intake of fluid and a diet free of all condiments and other irritating substances.

* At the base hospitals in France the use of atropine ointment, instead of liquid paraffin, is adopted when the cornea is hazy or otherwise injured.

In all of these local lesions a predominating characteristic was the frequency and persistence of the neurotic symptoms. These rendered the treatment of the after-effects of mustard gas poisoning most difficult. But it was found that as soon as the treatment of the symptoms was approached from this point of view, they improved very rapidly, and, in the majority of cases, completely. The lack of realisation of this fact rendered the cases most obstinate and difficult of control.

None of the local lesions except the vomiting interfered with the patients' prompt return to duty. There was, however, one group of symptoms which outnumbered all others, both in frequency and severity, namely, those of the condition commonly called D.A.H., or the effort syndrome, as already described. These were most common in phosgene poisoning, but also occurred in a significant number of the mustard gas cases. Rest in bed was absolutely contra-indicated. If the patient complained of severe symptoms, or if he were too fatigued to accomplish any exertion, he was placed in a wheel chair and made to spend as much time as possible in the open air. He was encouraged each day to take a few more steps until he was able to walk without distress. As soon as possible the patient was placed on graduated physical exercise, as used in the treatment of D.A.H. Various additional methods of treatment are being tried in order to overcome the rapid and shallow respiration. The results of these will be reported in a future communication. The most difficult patients of this variety to treat were those who had been confined to bed for a considerable period, either in France or in the United Kingdom.

Period in Hospital.—The majority of the cases were received direct from France, where they had been in hospital for an average period of 14 days, varying from one to 13 weeks (Table 5), while a certain number of the cases came under our care after they had been treated in other hospitals in the United Kingdom. There was a considerable variation in the duration of symptoms. In the mustard gas cases 65 per cent. were fit for discharge before the end of the fifth week of treatment in the United Kingdom ; while only 35 per cent. of the phosgene cases were discharged during this period.

TABLE 5.

	Weeks.																		Over 18 weeks.
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	—
Mustard Gas—																			
In France ...	45	30	12	6·5	4	—	1·5	—	0·5	—	—	—	0·5	—	—	—	—	—	—
In U.K. ...	5·5	14	15	20·5	10	7·5	2	1	9	0·5	2	1	3	—	2	—	2	—	2
Total ...	—	2	10	14	14	20	8	6	5	4	2	2	2	2	2	1	2	1	2
Phosgene—																			
In France ...	55	7·5	15	11	7·5	—	4	—	—	—	—	—	—	—	—	—	—	—	—
In U.K. ...	14	3·5	3·5	14	—	7·5	3·5	3·5	10·5	—	—	—	3·5	—	—	—	—	—	36·5
Total ...	—	3	6	3	15	3	9	6	3	3	3	3	1	2	2	1·5	—	—	36·5

Period in hospital in France, in United Kingdom, and total stay. (Percentages).

The phosgene cases were, on the average, much more resistant to treatment than the mustard gas, 36.5 per cent. of them required more than 18 weeks' treatment before they were considered fit for discharge. If the total period in hospital is considered, combining the period in France with the period in the United Kingdom, it is found that 77 per cent. of the mustard gas cases were discharged before the end of the seventh week, while only 43 per cent. of the phosgene cases were discharged in the same period. The cases of mustard gas poisoning admitted during the late Autumn of 1917 and the Spring of 1918 have been of a much milder type, and the majority have required treatment for only one to two weeks before being discharged to full duty. It was found of great importance to discharge those cases with mild or no symptoms as early as possible.

Symptoms prolonging the stay in Hospital.—The symptoms which prolonged the total stay in hospital over seven weeks varied somewhat for the different gases. This diversity was of degree rather than of variety, between phosgene and mustard gas (see Table 6). In the cases of phosgene poisoning by far the most important group was that of D.A.H. or the effort syndrome, and of the symptoms of this condition dyspnœa was the most important. In only two cases was another group of symptoms, namely, vomiting, &c., responsible for a prolonged stay in hospital. In the mustard gas cases, besides the symptoms of D.A.H., vomiting, conjunctivitis and burns, accounted for a small number of cases.

TABLE 6.

Gas and Total Number.	Dyspnœa.	Chest pain.	Præcordial pain.	Cough.	Tachycardia.	Vertigo.	Conjunctivitis.	Fatigue.	Vomiting.	Burns.	Miscellaneous causes.
	Per cent.	Per cent.	Per cent.	Per cent.	Per cent.	Per cent.	Per cent.	Per cent.	Per cent.	Per cent.	
Mustard, 56 cases, 34 per cent.	55	18	23	29	20	12·5	9	7	11	7	1. Laryngitis, functional, cured in 10 minutes 1. Keratitis 1. Pleurisy with effusion, and corneal ulcer 1. Severe conjunctivitis due to Bell's Palsy 1. Extensive bronchitis and emphysema
Phosgene, 19 cases, 58 per cent.	89·5	5	58	21	58	42	—	14	10	—	1. Pulmonary tuberculosis

Symptoms directly resulting from gas poisoning which necessitated stay in hospital (France and England) over seven weeks.

Disposal of Cases.—The disposal of patients to the various forms of duty and convalescence is set forth in Table 7. This was determined by the capacity of the patients to accomplish physical exercises, as instituted at the Hampstead Military Hospital for affections of the heart (D.A.H.)

Mustard Gas.—There were discharged to duty 132 cases (81 per cent.) of mustard gas poisoning, and the great majority were sent to command depôts (Furlough II), as it was considered that the regimental discipline exacted would be of great value in overcoming the neurotic condition which was present in so many of the cases. Two cases were lowered in category, as it was considered that they would not be fit for full duty for some time, and that they could perform duties suitable for B Class men. One of these cases had been subject to frequent attacks of bronchitis before being gassed. After that event the bronchitis was persistent, but only partially interfered with his duties. The other case suffered from a right-sided Bell's palsy, dating from birth. The right eye had been very severely affected at the time of being gassed, and a pronounced purulent conjunctivitis followed. After this had been cured his eye was very sensitive to any irritation, especially dust from the road, and exacerbations of the conjunctivitis readily occurred. Apart from this local condition he was in good health. It was therefore considered advisable to discharge him to light duty until such time as the conjunctiva should recover from its abnormal sensitiveness. One of the mustard gas cases was admitted to another hospital near his home while on Christmas leave. He was a case with moderate D.A.H. symptoms, but was of a pronounced neurotic temperament.

Five cases of mustard gas poisoning (3 per cent.) were discharged from the army as permanently unfit for further military service for the following reasons :—

1. Pte. M.—Tuberculous pleurisy and recurrent corneal ulcers, probably tuberculous.

2. Pte. W. E.—Bilateral detachment of the retina with almost complete blindness—had antedated gassing, but seemed to be aggravated by it.

3. Pte. P.—Extensive chronic bronchitis and emphysema following very severe gas poisoning.

4. Pte. H.—Persistent vomiting.

5. Pte. M.—Persistent vomiting.

It will be seen that it was exceptional for a case of mustard gas poisoning to be permanently unfit for further military duty as the result of the direct action of the gas. Cases 4 and 5 were definitely neurotic in type, and although at times apparently cured, they had repeated recurrences of the vomiting.

Phosgene.—Seventeen cases of phosgene poisoning (51 per cent.) were discharged to duty. One of these cases was discharged in Category B, which was the same as on admission. He had been serving in France in a Labour Battalion on account of a gun shot wound of the foot, which he had received a year previously.

Ten cases of phosgene poisoning (30 per cent.) were discharged permanently unfit. The causes for this classification were as follows :—

1. Lieut. B.—Severe dyspnœa, palpitation, and cyanosis on the least exertion. Severe attacks of nocturnal dyspnœa.

2. Pte. S. W. C.—D.A.H. and neurasthenia.

3. Pte. A. S. C.—D.A.H. and neurasthenia.

4. Pte. H. F. D.—Pulmonary tuberculosis.

5. Pte. A. R. D.—D.A.H. and asthma, result of gassing.

6. Pte. S. W. J.—D.A.H. and neurasthenia.

7. Pte. C. L.—D.A.H. and neurasthenia.

8. Pte. G. L. T.—Severe dyspnœa on exertion and attacks at night. Severe D.A.H.

9. Pte. L. G. G.—Persistent vomiting.

10. Pte. M. S.—Persistent vomiting and D.A.H.

It will be seen from these cases that the most frequent cause of permanent disability after phosgene poisoning is D.A.H. and neurasthenia. The neurotic element is a dominant one in that it appears not only with D.A.H. symptoms, but also is manifested in two cases of persistent vomiting of a functional character, and in the case of asthma which was quite typical of that form due to a neurosis.

There is a striking similarity between the causes of permanent unfitness in these two kinds of gas poisoning. The great preponderance of the D.A.H. symptoms in the phosgene cases throws a striking side-light on the initial cause of these symptoms, namely, deficient oxygenation of the blood, causing "oxygen want." This is almost constant and frequently severe during the earlier stages of phosgene poisoning, with the consequent far-reaching and sometimes almost permanent disablement. In mustard gas poisoning, where œdema of the lungs is not frequent and where the "oxygen want" is of a less pronounced degree, the same permanence of these symptoms is not found to occur.

In three cases which were gassed with chlorine in 1915, and who came under our observation during the past six months, it was necessary to discharge as permanently unfit. One suffered from severe D.A.H. and two from pronounced bronchitis and emphysema. These cases form an important connecting link between the two other forms of gas poisoning, as chlorine acts both like phosgene as a suffocative and also like mustard gas in having an intensely irritant action on the main bronchial passages.

TABLE 7.

Disposal.	No. so disposed of	Ultimate Fate.						
		B.E.F.	A.	B.	C.D.	Other Hosp.	P.U.	Not heard from.
Fur. I.	21	1	7	3	—	—	—	10
Fur. II.	109	17	41	3	19	10	1	18
Fur. III.	2	—	—	2	—	—	—	—
Con. Hosp. ...	25	—	9	6	4	2	—	4
Other Hosp. ...	1	—	—	—	—	1	—	—
Per. Un.	5	—	—	—	—	—	5	—
Totals	163	18	57	14	23	13	6	32

Disposal and ultimate fate of Mustard Gas cases.

TABLE 8.

Disposal.	No. so disposed of.	Ultimate Fate.						
		B.E.F.	A.	B.	C.D.	Other Hosp.	P.U.	Not heard from.
Fur. I.	7	6	1	—	—	—	—	—
Fur. II.	9	3	2	3	1	—	—	—
Fur. III.	1	—	—	1	—	—	—	—
Con. Hosp. ...	6	2	2	1	1	—	—	—
Per. Un.	10	—	—	—	—	—	10	—
Totals	33	11	5	5	2	—	10	—

Disposal and ultimate fate of Phosgene cases.

TABLE 9.

Case No.	Symptoms.	Case No.	Symptoms.
62	Dyspnœa, palpitation and fatigue	142	Dyspnœa, palpitation, fatigue
39	Loss of right thumb	162	Chronic double otitis media following concussion
28	Unknown	170	Conjunctivitis and Bell's palsy
113	Cough and dyspnœa	164	D.A.H. and debility
114	Cough and dyspnœa with expectoration	*14	General debility and fatigue
68	Vomiting, cough and dyspnœa	*36	Unknown
103	Dyspnœa and bronchitis	*4	G.S.W. foot
131	Unknown	*13	Neurasthenia and bronchitis
42	Pain in chest and dyspnœa	*12	Dyspnœa, tachycardia, bronchitis
119	Unknown		

Cases reduced in Category. (* Phosgene cases.)

TABLE 10.

Case No.	Symptoms.	Case No.	Symptoms.
98	No symptoms	133	Dyspnœa and tachycardia. Cannot wear respirator
79	Dyspnœa and vomiting	66	No symptoms
27	Dizziness, dyspnœa, chest pain and fatigue	105	,, ,,
161	No symptoms	75	,, ,,
130	,, ,,	67	,, ,,
48	Considerable dyspnœa	43	,, ,,
138	Tachycardia and dyspnœa	155	,, ,,
136	Headache and dizziness	122	Chronic bronchitis and Dyspnœa
64	Chronic bronchitis. Tb ?	70	No symptoms
139	No symptoms	83	,, ,,
96	Chronic bronchitis	46	,, ,,
*29	Tachycardia, dyspnœa and palpitation on exertion	20	Severe cough, hæmoptysis and chronic bronchitis
*128	Dyspnœa on exertion		

Cases remaining in Command Depôts. (*Phosgene cases.)

TABLE 11.

Case No.	Symptoms.
100	Vomiting and gastritis
63	V.D.G.
152	Unknown
88	V.D.S.
50	Chronic bronchitis
99	Cough, pain in chest, dyspnœa, exhaustion and chronic bronchitis
24	Chronic bronchitis
112	,, ,,
101	Vomiting and bronchitis
61	Unknown
73	Gastritis
195	Dyspnœa, tachycardia
158	V.D.G., also slight bronchial and gastric catarrh with dyspnœa on exertion

Cases re-admitted to hospital.

Ultimate Fate.—All the cases were followed three months after discharge from this hospital. The main points of information sought were :—

(1) The patients' eventual classification.

(2) Their physical fitness as a soldier, and

(3) Such symptoms and physical signs as interfered with their performance of full duty.

Mustard Gas.—Of 163 cases discharged from hospital 130 have been followed to date. Of these 75 (58 per cent.) have returned over-

seas or are doing full duty in the United Kingdom. Twelve cases (9 per cent.) have been lowered in category and two (1·5 per cent.) remain in class B as on discharge. Twenty-three (18 per cent.) are still under treatment in Command Depôts, and 12 (9 per cent.) have been readmitted to hospital. Only one case has been discharged subsequently as permanently unfit for any form of military service, making the total number of such cases six (4.5 per cent.). It is therefore probable that 75 per cent. of mustard cases will be fit eventually for full military duty.

Phosgene.—In the phosgene cases all (33) have been traced. Of these 16 (50 per cent.) have proceeded overseas or are on full duty at home. Five cases (15 per cent.) have been lowered in category, and two (6 per cent.) are still under treatment in Command Depôts, while 10 (30 per cent.) have been discharged as permanently unfit for military duty. In tables seven and eight these results are summarised and tabulated. The main fact which emerges from these tables is the high degree of permanent disability of phosgene poisoning, and the low degree of disability due to mustard gas.

It was considered of importance to determine as far as possible the reasons for the reduction of category, continued stay in Command Depôts, and re-admission to hospitals. In Tables 9, 10 and 11, the findings are tabulated in full. The symptoms given are those which were reported by the Medical Officer in charge of the case at the time of enquiry. Many of these in Command Depôts were reported to be improving. It may therefore be presumed that a number of these cases will eventually be fit for full duty. Those who were re-admitted to hospital were very likely suffering from more pronounced symptoms than those who had been lowered in category and those who were still in Command Depôts. The most striking features of these reports are the great prevalence of chronic respiratory disorders, such as chronic bronchitis or dyspnœa associated with other symptoms of D.A.H., and the frequency of vomiting. These facts confirm the observations made when the patients were under our care. It is of interest to note the prevalence of chronic bronchitis. As noted above certain cases while under our observation for a prolonged period eventually developed bronchial signs which were suggestive of asthma. The râles, after they had developed, continued to be present constantly up to a certain degree. It was only by close observation that the periods of exacerbation were detected although the patients frequently complained of periods of increased difficulty of breathing, which were not sufficiently acute and severe for them to describe them as definitely asthmatic. It therefore seems likely that some of these cases of chronic bronchitis may be of this character.

(*For help in the preparation of the statistical material from the clinical notes we wish to express our thanks to Captain J. G. Priestley, M.C., R.A.M.C.*).

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CHEMICAL WARFARE MEDICAL COMMITTEE.

No. 8.—REPORTS ON FATAL CASES OF POISONING.

(i.) ETHYL IODOACETATE.

June 1918.

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REPORT ON POISONING BY ETHYL IODOACETATE.

By Frank Shufflebotham, M.D.

Poisoning by Ethyl Iodoacetate.

Ethyl Iodoacetate is a colourless oily liquid with a boiling point of 180° C. The symptoms of poisoning by this body are mainly those of lachrymation and local irritation of the eyes, as well as irritation of the respiratory tract; while in severe and fatal cases, intense congestion of the lung with œdema are found in addition to inflammatory changes in the kidneys.

Exposure to the fumes of ethyl iodoacetate causes the most profuse lachrymation and, in severe cases or with further exposure, conjunctivitis and blepharitis are set up. Persons suffering from astigmatism or other refractory errors or conditions which predispose to conjunctivitis, are more easily and more severely affected than other people.

A splash of the liquid into the eye may produce a serious attack of conjunctivitis, and keratitis has been set up in some instances with a resulting corneal opacity.

The fumes of ethyl iodoacetate often cause blistering of the skin, and the handling of the liquid may produce eczematous ulceration of the skin over the hands and wrists. Cases of blistering of the skin over the arms and shoulders and even on the chest may arise among workpeople at factories and filling stations on account of the fumes having passed up the sleeves of the workers' clothes.

Abrasions of the skin as well as scratches and contusions invariably become septic when exposed to the fumes of this body, and this fact is of the highest importance because septic poisoning with serious results so frequently sets in as a result of such exposure. I have seen many cases of septic fingers with cellulitis of the arm resulting from the smallest scratch after being exposed to these fumes. When the abrasions occur on the face the results may be of a still more serious nature.

The effects of the fumes on the respiratory tract may be shortness of breath with a cough and expectoration and cases of laryngitis may result in this way.

In more severe cases, inflammation of the trachea, bronchi and bronchioles may set in, and in other cases one may find œdema of the lung or pneumonia. An emphysematous condition may be a resulting factor.

In cases where the lachrymation has been excessive, suppression of urine has followed, and in one instance which came under my notice suppression continued for 20 hours after exposure to the fumes. In some instances there may be definite congestion of the kidneys with albuminuria.

Fatal Case of Poisoning by Ethyl Iodoacetate.

A workman was badly gassed through the explosion of a shell containing this substance, and he died on the same day from severe inflammation and congestion of the trachea and lungs due to the irritation of the fumes.

A post-mortem examination was performed by Dr. R. C. Wingfield, and the general post-mortem notes were as follows :—

The body was that of a well nourished man. The face was generally swollen, especially the eyelids and the conjunctiva of both eyes was intensely congested. The mouth appeared to be normal.

On opening the thorax it was seen that the right lung showed advanced emphysema along the anterior border which stretched across the middle line. There were dense pleural adhesions on the left side and slight adhesions on the right side.

The *right lung* was bulky and somewhat solid to the touch. On examination it was found to be intensely congested and œdematous, but no solid areas could be found. The œdema and congestion were equally marked throughout the lung, although the tendency to consolidation appeared to be greater in the lower lobe.

The *left lung* was congested, the congestion being more advanced in the upper lobe. There was but little œdema of this lung, which was not bulky, and in which there were no solid areas.

The *Larynx.*—The mucous membrane of the larynx was hyperæmic and œdematous. There was inflammatory swelling of the base of the glottis, of the arytenoid cartilages as well as of the vocal cords.

The *Trachea.*—There was acute inflammation of the trachea along its whole length, and this inflammation was most intense at the bifurcation, where it was deep red in colour, swollen and there was a viscid purulent excretion covering the surface. On following up the bronchial tree the inflammation increased in degrees as the finer air passages were reached.

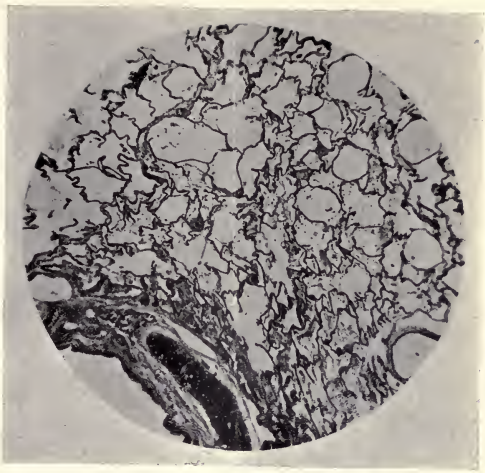
The *Heart.*—The pericardium was normal. The endocardium and heart muscle were normal, but there was some early disease of the coronary atreries.

The *kidneys* showed signs of congestion. The liver, spleen and peritoneum were normal, and the brain and contents of the cranial cavity only showed a slight increase in the amount of cerebro-spinal fluid under the lateral ventricles and some congestion of the choroid plexus.

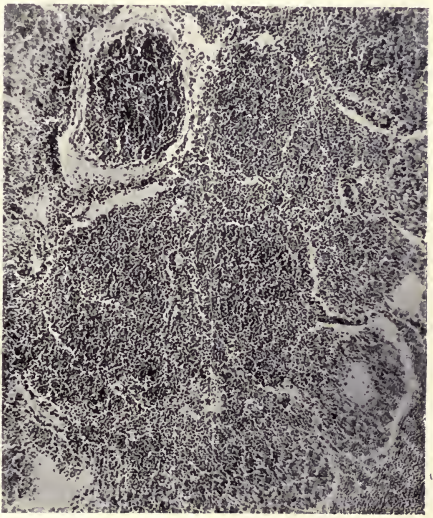
The *bladder* was contracted and contained less than an ounce of urine.

Specimens were taken for microscopical examination from :—

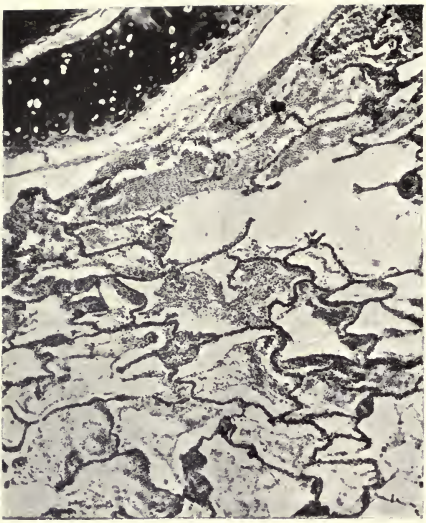
(1) Lungs,
(2) Trachea,
(3) Bronchi,
(4) Liver, and
(5) Kidneys.



1. *Lung.*—Showing an obvious degree of disruptive emphysema and capillary congestion.

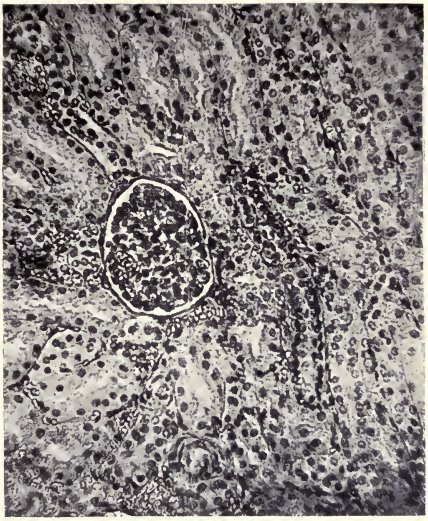


2. *Lung.*—Showing the tissue to be practically solid, the alveoli being packed with red cells.

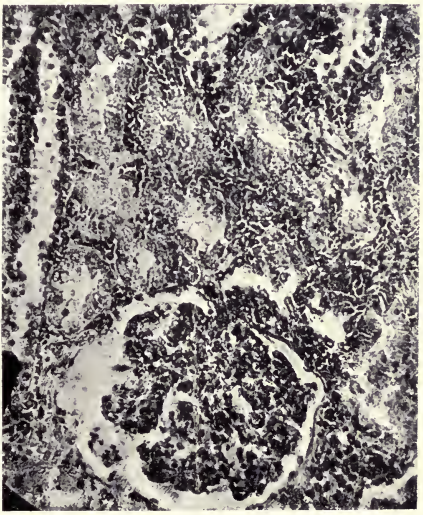


3. *Lung* (high power).—Showing distension and bursting of the alveoli, congestion of the capillaries and red cells extravasated into the alveoli.

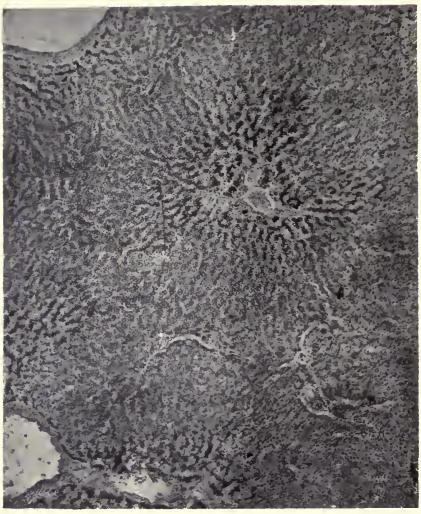
4. *Tracheal Wall.*—Showing submucous swelling and infiltration with inflammatory cells. The mucous membrane with its epithelial cells is still present, but the cells are much damaged. The section shows a distended vessel.



5. *Kidney.*—Showing a normal glomerulus and patchy degeneration of the tubular epithelium.



6. *Kidney* (high power).—Showing some degeneration and desquamation of the cell lining. Bowman's capsule and disintegration of the tubular epithelium.



7. *Liver.*

This examination was carried out by Dr. Wingfield, who reports in the following terms :—

Description of Microscopic Specimens.

Lungs, Right Upper Lobe.—In this lobe we find a certain degree of emphysema and intense capillary congestion, with early and slight extravasation of red cells into the alveoli. There is no marked œdema. A cross section of one of the finer bronchioles shows an intense inflammation, the wall being densely infiltrated with finely granular oxyphil leucocytes, and in the lumen is a plug composed of extravasated serum packed with finely granular oxyphil leucocytes and large mononuclear leucocytes. (*See* Figs. 1 and 3.)

Right Lower Lobe.—This part of the lung is practically solid with blood. Each alveolus is tightly packed with red corpuscles. The capillaries are intensely overfilled. In this section there is unfortunately no creditable cross-section of a bronchiole, but a broken one is seen filled with blood and finely granular oxyphil leucocytes. (*See* Fig. 2).

Left Upper Lobe.—In the left upper lobe we have much the same picture as that of the right upper lobe, save that the congestion is not so well marked. In one or two places there is some œdematous fluid in the alveoli.

Trachea.—The mucous membrane is in places destroyed and missing, where it is left the cells are either dead or greatly destroyed. There is œdema of the submucosa, and it is intensely congested with early extravasation of red corpuscles into the tissues. The submucosa is infiltrated with finely granular oxyphil leucocytes, large mononuclear leucocytes and plasma cells, and the passage of these to the surface is well shown. (Fig. 4.)

Bronchiole.—A cross-section of one of the larger bronchioles shows the same pathological features as the piece of trachea, save that the extravasation of red corpuscles under the mucous membrane is more marked, and the infiltration with finely granular oxyphil leucocytes penetrates the wall more deeply.

Kidneys.—These sections show marked congestion.

The glomeruli beyond having their tufts somewhat over distended show no special change.

The tubules show epithelial damage. The cells in most places are swollen and distinctly granular, and in some part complete nuclear disintegration has occurred. (Figs. 5 and 6).

Liver.—This organ is not congested. The liver cells show distinct cloudy swelling. There is a well marked deposit of pigment, probably bile, in the liver cells, most marked in the centre of the lobule surrounding the central vein, a branch of the hepatic vein. The liver sinuses appear to contain an undue proportion of finely granular oxyphil leucocytes. (Fig. 7.)

General Remarks.

The gross effects of this gas may be summed up thus :—

Its exhibition in strong concentration causes an acute hæmorrhagic conjunctivitis of such intensity that it is probable that it would have

permanent effect on the eye—in the shape of corneal opacities, and might even have the immediate effects of acute septic inflammation of the whole organ.

Its inhalation though more or less innocuous to the coarser tissues of the mouth, nose and pharynx, causes inflammation with œdema of the larynx and acute inflammation, growing more marked as it proceeds downwards, of the trachea, bronchi, bronchioles and alveoli.

The immediate cause of death in the fatal case above described was asphyxia caused by the obstruction of the bronchioles and finer passages by inflammation and inflammatory products—for it was noticed that even in the less affected lung the bronchioles that could be seen were intensely inflamed while pressure produced small beads of purulent exudate from the finer tubes which could not be recognised with the naked eye.

The right lung suffered more than the left, and the lower lobe more than the two upper ones. This is probably explained by the fact that owing to the dense pleural adhesions in the left side, and the slighter, but still well marked, ones over the right upper lobe, the right lung and more especially its lower lobe, were chiefly used by this man for breathing.

The extra work thrown on the right lung was clearly demonstrated by the marked emphysema seen in it when the chest was first opened.

The kidneys present a more intricate problem. The man passed no urine between the time of his admission to the hospital at 8 a.m., and his death at 1.15 p.m., nor did he secrete much during that time, as his bladder was contracted and contained less than an ounce of urine.

This is not surprising when we see the changes in the renal epithelium. But is this damage caused by the congestion of slow asphyxiation or by direct toxic action of the gas or some by-product of the gas in the blood? One can only venture an hypothesis that, as congestion was not a marked feature in the liver or spleen, the renal congestion and epithelial damage were probably due to direct toxic action.

I can see no way of settling this question other than by animal experiment, although I have already referred to suppression of urine and albuminuria in connection with poisoning by this body. Under these circumstances I believe it might be permissible to say that this body has a direct toxic action on the kidneys. The cloudy swelling of the liver cells, bears out the suggestion of some toxin circulating in the blood, but I am at a loss to account for presence of an increased number of finely granular oxyphil leucocytes in the liver sinuses.

Treatment.

(*a*) *Preventive.*

Suitable goggles and respirators should be worn by all persons who may be exposed to fumes of ethyl iodoacetate.

Workpeople employed in the manufacture of this body and those engaged at filling stations should wear overalls with straps around the wrist so as to prevent the fumes passing up the sleeves, and girls and

women so employed should not wear low-necked blouses, otherwise the skin over the neck and chest may be affected. It is advisable to lubricate the hands with an antiseptic ointment so as to prevent irritation of the skin.

Cases of suspected astigmatism or other refractive errors should be examined with a view to correction by spectacles.

(*b*) *Curative.*

The curative treatment may be considered from two points of view :—(1) whether the case be mild, or (2) whether it be serious.

(1) *Mild Cases.*—All cases of conjunctivitis should be treated by washing the eye twice daily with a 1 per cent. solution of protargol. In ordinary cases this treatment is successful in three or four days' time, and the result is most striking even in the severest type of case when there is suppression or when the cornea is affected. When there is suppurative conjunctivitis, boracic fomentations are useful in addition to the protargol treatment, and in these cases the eye should be shaded.

Blistering of the skin over the arms is best treated with antiseptic powders, and eczematous ulceration by antiseptic ointments.

Headaches are relieved either by aspirin or phenacetin and caffein.

Even the slightest scratches and abrasions among ethyl iodoacetate workers must be treated without delay. The affected part should be thoroughly cleaned, painted with tincture of iodine and dressed with a suitable dressing, and the case should be kept under constant observation until complete healing takes place. Septic infection should be treated by the ordinarily recognised methods.

Laryngitis and bronchitis should be dealt with in the usual way.

(2) *Severe Cases.*—Where severe lung trouble ensues, the patient must be treated along the lines laid down for poisoning by other lethal bodies which cause pulmonary irritation :—

Removal from the vitiated atmosphere.
Rest and warmth.
The administration of oxygen.
Bleeding in suitable cases.

When suppression of urine takes place, a hypodermic injection of pituitrin (in doses of ·5 cc.) often gives relief.

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